Comments on the "*one big question*"

„HOW DOES HIV-1 CAUSE AIDS?“, Coffin und Swanstrom (2013)

Comments on the state of research on HIV with special consideration of the PCR method

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1. Introduction

This is about the "*one big question*", how the HI virus causes AIDS, starting from

"HOW DOES HIV-1 CAUSE AIDS? A*s is apparent from this article and the rest of the collection,* ***in the 25+ years since its discovery****, we have learned an enormous amount about HIV,* ***but we still cannot answer the one big question****: How does HIV-1 cause AIDS?"*

- From Coffin and Swanstrom in "*HIV Pathogenesis: Dynamics and Genetics of Viral Populations and Infected Cells*", Cold Spring Harb Perspect Med. **2013** Jan; 3(1), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3530041/

To begin the discourse, yes, there was the Holocaust. The videos of the Eichmann trial in Jerusalem in 1961 are authentic, see for example https://www.youtube.com/watch?v=Dp7iSy9cRmo. There are no aliens. There are viruses. There are successful vaccinations. I myself was vaccinated against polio, tetanus, diphtheria, TB and multiple times against flu, I had measles and chickenpox, and my immune system was successfully trained against tree pollen and grass allergy with a dehyperallergisation therapy. Einstein's Special Theory of Relativity has been confirmed in all (!) experiments.

Only people who have witnessed the AIDS hysteria of the 1980s and 1990s can understand the current situation and the astonishment given the still rudimentary understanding of the foundations of HIV / AIDS. And this in view of the catastrophic treatment results. To understand the situation, the following video from 1992 is recommended, https://www.youtube.com/watch?v=3H8kmwK2UrI. Both sides have their say[1].

This text brings together information from around ***600*** scientific publications on the subject of HIV/AIDS. When reading these publications, it should be noted that they were (almost) all written under the dogma that the HI virus is the cause of AIDS. Any other statement would have led to the immediate rejection of the publication, or the scientific integrity would have been attacked directly, regardless of any argument. Two examples for this follow later.

[1] I am only concerned with the film by Fritz Poppenberg from 1992. Unfortunately, health topics are increasingly being occupied by interest groups of all kinds. Not always in the interest of the patient. Profiteering does not only exist in the pharmaceutical group.

2. Summary

- It is very doubtful that the HI virus groups originate from at least ***13*** almost simultaneous zoonoses in Africa around ***1930*** as new, supposedly deadly pathogens for humans and that this was caused almost simultaneously by cross-species transmission to humans from at least ***3*** different animal species, namely chimpanzees (*SIVcpz*), gorillas (*SIVgor*) and sooty mangabeys (*SIVsmm*), with the formation of the virus groups HIV-1 and HIV-2.
- The SI virus has been found in 40+ species of apes and monkeys and exists for several million years. SIV is harmless. The same applies to other *lentiviruses*, which occur among other things in rabbits, cats, sheep, goats and cows.
- The theory of ***13*** very recent zoonoses is even more doubtful as the two presumed pathogenic virus groups, HIV-1 and HIV-2, differ by more than 45% in their genome.
- Equally questionable is the statement that this African virus first appears in the ***1980***s in a severely ill, often multiple classically infected (*syphilis*, *gonorrhea*, *HBV*, *herpes*, *CMV*, ...) and drug-dependent population in the USA. However, the virus hypothesis of AID syndrome has been developed on the basis of this population.
- Even after 35 years, the HI virus hypothesis of the *AID Syndrome* and the model of AIDS as a transmissible disease cannot explain many phenomena at the molecular level but also in the observed HIV/AIDS statistics.
- The CD4 cell count has proven to be a completely unusable measure of the immune status.
- Until today it is completely unclear how the HI virus can destroy *uninfected* CD4 cells. Only about 5% of the CD4 cells are infected, but also the not infected cell die and CD4 cells are reproduced in large numbers each day (*bystander cell enigma*).
- The *in vitro* analysis of retroviral activity requires specially activated cells for which there is no equivalent *in vivo*.
- There is still no animal model for AIDS (apes do not get AIDS).
- HIV antigen (Ag) and antibody (Ab) tests show a large variety of cross-reactions, especially in classical infections. This is not only relevant for developing countries. In addition, it is difficult to distinguish between endogenous (HERV) and exogenous (HIV) retroviral components.
- The diagnostic problem of the antigen (Ag) / antibody (Ab) tests continues with PCR. There are considerable doubts about the specificity of the PCR method.
- Manufacturers strictly reject the use of PCR for HIV diagnosis. And for a good reason.
- The antiretroviral therapy (ART) causes severe adverse effects. In particular, people taking ART suffer from cardiovascular damages, nerve damages as well as severe kidney and liver damages. People taking ART age prematurely. As a long-term consequence cancer is a thread. 75 – 90% of "*AIDS death*" do not die from AIDS defining diseases.
- The side effects of ART correspond 1:1 to the symptoms of ad-hoc defined *HIV-related diseases* in contrast to the around ***30*** AIDS-defining diseases that should appear after **10 - 15 years** (*lentivirus*).

- Up to 82% of those treated with ART suffer from these *non-HIV co-morbidities*. Up to 50% suffer from several *non-HIV co-morbidities*.
- The numbers on the *AID Syndrome* from Africa are greatly exaggerated and contributions from malnutrition, parasites or classical infections such as tuberculosis or malaria are included without testing. Tuberculosis is AIDS defining. Likewise are weight loss, prolonged fever and diarrhea, although completely unspecific, also AIDS defining. This makes any statistic on the *AID Syndrome* unusable.
- Prematurely new biomedical techniques have been introduced, without realizing the downsides and analyzing all risks beforehand.
- There is a lot that science just does not know for sure. HIV research depends on unproven, sometimes not even plausible assumptions. That did not prevent a whole HIV/AIDS industry from developing. Much of it has been developed on the living object, i.e. human beings.

3. Comments on the current situation

I hold the greatest recognition and respect for the individual scientist in molecular biology, biochemistry or microbiology. However, I also think that as a group (of molecular biologists, virologists, hematologists, ...) they have totally and completely failed[2]. And this in two ways.

On the one hand, they have allowed personally staged campaigns against individual scientists and have only tolerated people in the community who have been (and still are) sufficiently useful to the pharmaceutical industry. On the other hand, it has been accepted uncritically that new methods have been hastily approved and used (in particular PCR), without the weak points having been adequately investigated ("*There is nothing like a free lunch*"). On these two points in detail:

a) I am not aware of any science other than molecular biology (including adjacent areas) that would have tolerated a public crucifixion of the kind expressed in the editor's note for an article in 2007. Cf.

- Duesberg, „Chromosomal Chaos and Cancer", Scientific American, May **2007**, https://www.researchgate.net/publication/6332530_Chromosomal_Chaos_and_Cancer

"***Editors' note***: *The author, Peter Duesberg, a pioneering virologist, may be well known to readers for his assertion that HIV is not the cause of AIDS. The biomedical community has roundly rebutted that claim many times. Duesberg's ideas about chromosomal abnormality as a root cause for cancer, in contrast, are controversial but are being actively investigated by mainstream science. We have herefore asked Duesberg to explain that work here. This article is in no sense an endorsement by SCIENTIFIC AMERICAN of his AIDS theories*."

Yes, he knows retro viruses and cancer, but no, he does not know retro viruses and AIDS?

Also, I am not aware of a science that would have tolerated a smear pamphlet against a member of their community of the following nature (here in the medical section):

- S. Kalichmann, Front. Public Health, 13 February **2015**, Commentary on "*Questioning the Hiv-AIDS Hypothese: 30 years of di*ssent", https://www.frontiersin.org/articles/10.3389/fpubh.2015.00030.

Note: Mr. Kalichmann earns his money through HIV / AIDS research funding, currently 5 contracts (grants) cf. https://chip.uconn.edu/person/seth-kalichman-phd/#

Especially those who call for a peer review process for minority opinions have had no problem with the Heckler / Gallo approach from 1984 without any peer review. Nor do they have a problem with censorship of minority opinions, cf.

- Schüklenk, "*Professional responsibilities of biomedical scientists in public discourse*", J Med Ethics. **2004** Feb; 30(1): 53–60, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1757140/pdf/v030p00053.pdf

May the public not know what science is arguing about? Or is that only possible after a pre-filtering? Maybe the population may also learn what science does not know? At any rate, a unified opinion as a scientific principle does not sound very scientific.

[2] I would like to exempt the German science a little bit, since the substantial influence came from the USA. I do not think anyone was aware of the paranoid state of US society as a whole. The effect in Germany, however, was that mediocrity became the standard in biomedical research. Those who shouted the loudest "*HIV*" were usually appointed to appropriate university positions. However, the German medical profession was never known for critical spirit.

It remains unclear why an editor is dismissed when a dissenting opinion is expressed in a scientific magazine, cf.

- Enserink, "*Berkeley Drops Probe of Duesberg After Finding 'Insufficient Evidence'*", Jun. 21, **2010**, http://www.sciencemag.org/news/2010/06/berkeley-drops-probe-duesberg-after-finding-insufficient-evidence

and

- Duesberg et al., "*WITHDRAWN: HIV-AIDS hypothesis out of touch with South African AIDS - A new perspective.*" Med Hypotheses. **2009** Jul 19, https://www.ncbi.nlm.nih.gov/pubmed/19619953

on the peer review process. Somewhat strange that someone is denied the opportunity to defend himself against the accusation of being responsible for the deaths of 330,000 people, cf.

- Duesberg et al., "*HIV-AIDS hypothesis out of touch with South African AIDS - A new perspective.*", **2009**, http://www.duesberg.com/2009_Duesberg_et_al_Medical_Hypotheses.pdf.

and

- Duesberg et al., "*AIDS since 1984: no evidence for a new, viral epidemic--not even in Africa*.", Ital J Anat Embryol. **2011**;116(2):73-92, https://www.ncbi.nlm.nih.gov/pubmed/22303636 and http://www.duesberg.com/articles/Duesberg%20et%20al_AIDS%20since%201984%20No%20evidence%20for%20a%20new%20viral%20epidemic%20not%20even%20in%20Africa_IJAE_2011.pdf

The allegations against Dr. Duesberg are completely unfounded. If 75% to 90% of patients do not die from the symptoms of the putative disease, but from symptoms that are strikingly similar to the side effects of the alleged medications, then you have a big problem. With misinformation and slander à la *Chigwedere et al.* you might fool the people for a while. But **you cannot fool all the people all the time**[3].

Dr. Duesberg defends the people amongst other things against the fact that the therapies on HIV / AIDS have cost millions of years of life and continue to cost. Cf.

- Jane Gross, "*AIDS patients face downside of living longer*", New York Times, 6 January **2008**; http://www.nytimes.com/2008/01/06/health/06HIV.html?pagewanted=all

"Mr. Holloway, who lives in a housing complex designed for the frail elderly, suffers from complex health problems usually associated with advanced age: ***chronic obstructive pulmonary disease, diabetes, kidney failure, a bleeding ulcer, severe depression, rectal cancer and the lingering effects of a broken hip****."*

Here's another example of a long term HAART survivor, a video on the Guardian's website from 2014, cf.

- The Guardian, „*Growing old with HIV: 'I'm in my 30th year of sickness. For the last 23, I've thought about death almost every day*'", **2014**, https://www.theguardian.com/society/video/2014/aug/14/hiv-america-us-aging-video

[3] We come back to the model calculation of Chigwedere et al., which is based on very crude assumptions in Chapter 20, *AIDS and Africa*.

Scott Jordan, the man in the Guardian was measured HIV+ in 1984. **He had none of the approximately 30 AIDS-defining diseases. He has not been cured of any of these diseases. He never had one**. Nevertheless, he takes 13 different drugs a day. Most of them today against the side effects of HAART.

(Scott Jordan, then 53 years old, after 30 years of HAART on his stair lift)

All this in the case of a disease that does not show any symptoms of its own and that must be looked at in an absurdly low concentration for the detection of fragments of individual molecules. There are strong doubts necessary because all of the symptoms of the suspected disease correspond to the side effects of the drugs used.

But here the Anti-Duesberg - Prof. Dr. med. Jürgen K. Rockstroh, Department of Internal Medicine I, Bonn, a very useful member of the scientific community.

Prof. Dr. Rockstroh is holder of the Federal Cross of Merit (with ribbon) and a welcome guest of the pharmaceutical industry. His "*conflict of interest*" statement lists 12 (!) of such conflicts, cf.

- Hensel et al. „HIV and Cancer in Germany“ Dtsch Arztebl Int **2011**; 108(8), https://www.aerzteblatt.de/pdf.asp?id=81038

*“**Conflict of interest**: Prof. Rockstroh: Consultancy (advisory board) and lectures for Abbott, BMS, Boehringer-Ingelheim, Gilead, GSK, MSD, Novartis, Pfizer, Roche, Schering-Plough, Tibotec, and Vertex.”*

If we assume 1000 € per HIV+ "*patient*" under HAART per month and if we accept around 3 million HIV+ measured persons worldwide under HAART (1.4 million in 2005), then we have an estimated turnover of 3 billion € per month or 36 billion € in sales of HIV HAART medicines per year. There are also other therapeutic agents against the side effects (see above, Guardian 2014) of about the same height. In addition there are diagnostic measures for therapy control. It seems realistic to assume an HIV (not AIDS!) related sales of 80 - 100 billion € per year worldwide. Mr. Rockstroh has powerful friends.

What interests does Mr. Rockstroh represent now? Those of his industrial friends or those of the patients?

The intense relationships between research, patient testing and industry seem to be the rule here. In his renowned **textbook** on organic chemistry, Jonathan Clayden speaks enthusiastically about the successful cooperation in the 90s, cf. J. Clayden "*Organic Chemistry*", p. 1482,

"The AIDS crisis led to cooperation between the pharmaceutical companies unparalleled since the development of penicillin during the Second World War. Fifteen companies set up an AIDS drug development collaboration programme and government agencies and universities have all joined in."

That seems naive. At some point, the pharmaceutical industry will expect a return on investment (ROI).

The current status emerged after having concentrated all efforts here, cf. the **textbook** of Cann, A., "*Principles of Molecular Virology*", 5th ed., Academic Press **2012**, p.109,

„Bacteriophages don't make people sick (very often - more about that later in the book), so they don't get much attention these days when ***the only way you can run a laboratory is to get lots of research grants for working on "important" viruses such as HIV****."*

Without HIV most of the **15.000 participants of the 2018 International AIDS conference in Amsterdam** would be out of business from one day to the other.

b) In biomedicine, thanks to new technologies, *trees have been growing into the sky* for decades, there has been no limit to what was claimed possible. On the other hand, it seems strangely double-faced to compare praise of supposed biomedical achievements in the popular press with articles in scientific journals (see also annex IV).

- He et al., "*While it is not deliberate, much of today's biomedical research contains logical and technical flaws, showing a need for corrective action.*", Int J Med Sci. **2018** Jan 19;15(4):309-322, https://www.ncbi.nlm.nih.gov/pubmed/29511367

"*Biomedical research has advanced swiftly in recent decades, largely due to progress in biotechnology.* ***However, this rapid spread of new, and not always-fully understood, technology has also created a lot of false or irreproducible data and artifacts, which sometimes have led to erroneous conclusions****.*"

"***Another major reason is that we are too rushed in introducing new technology into our research*** *without assimilating technical details. In this essay, we provide examples in different research realms to justify our points. To help readers test their own weaknesses,* ***we raise questions on technical details of RNA reverse transcription, polymerase chain reactions, western blotting and immunohistochemical staining****, as these methods are basic and are the base for other modern biotechnologies.*"

"*Many scientists have successfully established their career at a young age by introducing novel techniques into their research areas and publishing in high-impact journals,* ***while leaving the research fields with numerous artifacts and biased or erroneous conclusions.****"*

That's rather marked. One of the most noteworthy examples of this is PCR, which is ostensibly ultra-sensitive, but for that very reason leads to a number of serious problems (see below and Appendix II). At the

same time, and that goes by the board, it's an extremely stupid method, in the sense that PCR primers amplify everything (!) to which the primers can dock. The match does not have to be 100%, see also Annex II.

How is it possible that the following statement on the application of the RT-qPCR methodology can be read in **2018**? Cf.

- Sanders et al. "*Improving the standardization of mRNA measurement by RT-qPCR*", Biomol Detect Quantif. **2018** May; 15: 13–17, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6006386/

"Our recent review of the literature has shown that the qPCR data underlying the vast majority of publications reporting use of this technique are, at the very least, inadequately reported and that the peer review process allows the publication of ***incomplete experimental protocols, yielding results that are difficult to evaluate independently.*** *An analysis of all colorectal cancer publications that made use of qPCR between 2006 and 2013 shows* ***that only 3% (n=179) report sufficient experimental detail to allow a reliable assessment of the qPCR data****. That paper also showed that 92% of publications used a single reference gene,* ***with 13% validating its use and 92% of papers use a method of analysis that is meaningless unless PCR efficiencies are known, yet 82% do not mention PCR efficiency****. A more recent analysis found that 95% of papers (n=20) used a single reference gene for normalisation, with only 20% using a single validated reference gene.* ***Two other surveys found that 100% of papers (n=20) used inappropriate analysis and normalisation procedures****."*

But it is not just the application of the methodology that causes problems. There are also systematic errors. Here one seems to have completely overlooked that **DNA = DNA**, no matter what species. It has been proven that the smallest amounts of DNA fragments are enough to generate false signals in PCR. Thus, single DNA molecules from food that had been transferred from the intestinal tract into the serum were detected there by PCR, see also Appendix II. There are numerous **homologous DNA sequences**, both in human DNA, and in other species, that correspond to the DNA sequences of the putative HI virus. This may involve completely harmless bacteria or parasites, human DNA from the cells, or other residual serum DNA levels. Examples follow below.

A poorly understood and applied diagnostic approach, along with the AIDS hysteria of the 1980s and 1990s, gives for the suspected patient a very dangerous mix. In this respect one can see the personally tilted campaigns against the admonishers and the withdrawal of research funding for these persons as an expression of those methodical weaknesses. Forced scientific unification served (and serves) to discourage discordance from the beautiful new field of *molecular diagnostics*. Here HIV / AIDS seems only the first major case of a much deeper problem.

Meanwhile, one tries to counteract by combining different methods. The number of parameters to be considered increases exponentially. It is doubtful that the average family doctor still overlooks the current variety of methods. In view of the therapy methods, however, a "*we are still learning*" would be far too weak. It would be too late for Mr. Holloway, Scott Jordan and many others.

Maybe everybody would be helped, if we went over in Germany to a more graduated point of view and not take over 1: 1 any paranoia from the USA. Given the current therapeutic approaches, this would be much safer for the patient.

A note on the articles, which are referenced here, each with a link to the abstract or the article itself. In fact, every article starts by stating that HIV is the cause of AIDS, mostly in relation to WHO or UNAIDS figures (see below - AIDS and Africa). Then follows a more or less complicated middle part, which is usually followed by the closing statement, yes, we know a lot, but we have not quite understood this detail yet, further research is required. The research indulges in phrases like

- *could cause*
- *plays a role in*
- *presumably contributes to*
- *probably participates in*
- *is related to*

We have time. Bio markers everywhere and a very complicated concealment of the fact that science just does not know. But: plenty of opportunity (and money!) for new research. Each scientist sits in front of his or her molecule and diligently continues his or her research. If there was not HAART.

4. Current HIV therapy approaches and their consequences

It pays to dig deeper in the literature and look at what fits in with the term "*generally well-tolerated*" that HIV drugs are often given.

The current therapeutic approaches are based on combination of drugs with multiple nucleoside analogues and integrase and protease inhibitors. The application is based on the maxim "*hit hard and early*", i.e. the therapy should be started as early as possible and the drugs should be taken for the rest of the patient's life. For combination drugs, the price for a monthly pack is around € 1,000. (Since Aug 15th 2018 **SYMTUZA** is available in Germany for only **950.64 €/month** by prescription.)

HAART means Highly Active Anti-Retroviral Therapy. It consists of at least 3 cytotoxins, two of which are nucleoside analogues that cause chain termination and prevent cell division. Another cytotoxin is an integrase or protease inhibitor (see below).

AZT (azidothymidine or zidovudine) is used the longest. It comes originally from cancer therapy, is a nucleoside analogue and is found in many combination preparations (e.g., Combivir and Trizivir).

AZT (azidothymidine) is chemically similar to thymidine, one of the 4 basic building blocks of DNA (https://en.wikipedia.org/wiki/Thymidine) and part of many therapies (HAART). The following short explanation of the (presumed) mode of operation:

When a cell divides, each of the two daughter cells gets a full set of DNA again. For this purpose, the DNA strand must be doubled and it requires the basic building block thymidine. If azidothymidine (AZT) is present in the medium, it may be incorporated in the strand instead of the thymidine.

However, then the strand duplication is over (*chain termination*). The special feature of azidothymidine (AZT) is that afterwards the DNA strand cannot continue. But that also means that there is no DNA duplication, and the cell cannot divide.
AZT was originally developed in cancer therapy and the basic idea was that the rapidly dividing cancer cells are damaged more severely than the healthy cells. Unfortunately that did not work. There are similar chain terminators for guanine and cytidine, two more of the 4 basic building blocks of DNA.

It is widely agreed that AZT is a very toxic substance. In the US, it is classified as **carcinogenic**, cf.

AZT (Zidovudin) cancer: CHEMICALS KNOWN TO THE STATE [of California] TO CAUSE CANCER OR REPRODUCTIVE TOXICITY, as of Dec 29th, **2017,** https://oehha.ca.gov/media/downloads/proposition-65/p65122917.pdf

*„Zidovudine (AZT) cancer 30516-87-1 December 18, **2009**"*

AZT is so toxic that it should be used in chemotherapy, if at all, only for a short time, about 14 days. Here it did not have the desired effect. In the case of HIV+, as a secondary use, AZT should be taken for a lifetime.

The HIV book by Hoffmann and Rockstroh says to this:

- Hoffmann, Rockstroh, „*HIV 2016/2017*“, (sponsored by Gilead Sciences, Janssen-Cilag, MSD and ViiV Healthcare), https://www.hivbuch.de/wp-content/uploads/2017/04/hiv2016-17_fix.pdf

p. 530 on AZT (Zidovudin):

“*AZT ist seit Jahrzehnten in der Pädiatrie bewährt*.“

Translation:

"AZT has been proven for decades in pediatrics."

In addition to AZT, there are other nucleoside analogues that act (supposedly) according to the same principle:

Nukleoside	**Nukleoside analogon**	**Product name**
Guanosin	Abacavir	Ziagen®, Kivexa®, Trizivir®, Triumeq®
Thymidin	D4T	Stavudin®, Zerit®
Cytidin	3TC	Lamivudin®, Epivir®, Combivir®, Kivexa®, Trizivir®, Triumeq®
Cytidin	FTC	Emtricitabin, Emtriva®, also in Truvada®, Descovy®, Atripla®, Eviplera®, Odefsey®, Stribild® und Genvoya®

These "*active agents*" also come partly from cancer therapy and were only developed for short-term use (maximum of several weeks) in chemotherapy.

The side effects of AZT have been pointed out in the 80s and 90s again and again. Subjects in AZT studies (Concorde) showed significant damages of the bone marrow and survived only by blood transfusions. Already the initial phase of HIV / AIDS therapy cannot really be described as a success story, cf.

- Richmann et al. “*The Toxicity of Azidothymidin (AZT) in the Treatment of Patients with AIDS and AIDS related Complex*”, N Engl J Med **1987**; 317; 192 – 197, https://www.ncbi.nlm.nih.gov/pubmed/3299090

*“Although a subset of patients tolerated AZT for an extended period with few toxic effects, the drug should be **administered with caution because of its toxicity and the limited experience** with it to date.”*

- Kolata et al. “*Imminent marketing of AZT raises problems*”, Science, vol. 235, **1987**, p. 1462 http://go.galegroup.com/ps/anonymous?id=GALE%7CA4745577&sid=googleScholar&v=2.1&it=r&linkaccess=abs&issn=00368075&p=AONE&sw=w

- Chiu et al. ”*The toxicity of azidothymidine (AZT) on human and animal cells in culture at concentrations used for antiviral therapy*”, Genetica (**1995**) 95: 103, https://link.springer.com/article/10.1007/BF01435004

"However, after the licensing of AZT as an anti-HIV drug, several independent studies reported 20-to 1000-fold lower inhibitory doses of AZT for human and animal cells than did the manufacturer's study, ranging from 1 to 50 µM."

*"It is concluded that AZT, at the dosage prescribed as an anti-HIV drug, is **highly toxic to human cells**."*

- Axel Schock „*So groß die Hoffnung war, so schnell ist sie wieder verflogen*" in magazin.hiv, 20.03.**2017**, https://magazin.hiv/2017/03/20/so-gross-die-hoffnung-war-so-schnell-ist-sie-wieder-verflogen/

In the clinical trials on AZT the test persons only survived by blood transfusions, cf.

- Seligmann et al "*Concorde: MRC/ANRS randomised double-blind controlled trial of immediate and deferred zidovudine in symptom-free HIV infection*" Lancet **1994**; 343: 871-81, https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2894%2990006-X/abstract

"***The results of Concorde do not encourage the early use of zidovudine in symptom-free HIV-infected adults.*** *They also call into question the uncritical use of CD4 cell counts as a surrogate endpoint for assessment of benefit from long-term antiretroviral therapy*."

"*In all, 99 Imm and 38 Def participants **stopped trial capsules because of adverse events**. In only 16 Imm and 2 Def was haematological toxicity the main reason; in the rest it was predominantly gastrointestinal or neurological symptoms (headache) or malaise (table 6). **One or more blood transfusions were received by 18 Imm and 11 Def while they were taking trial capsules**."*

The harmful effects of AZT have been adequately studied and proven. There is no doubt that AZT (and other nucleoside analogues) not only hit the virus, but sustainably damage the normal cell division process. The damage has been proven to occur in at least 3 places, also at low doses:

Damage to thymidine kinase, an enzyme used to convert thymidine into a processable form for the human body (phosphorylation):

- Susan-Resiga et al. „*Zidovudine Inhibits Thymidine Phosphorylation in the Isolated Perfused Rat Heart*", Anti. A. Chemo., Apr. **2007**, p. 1142–1149, https://www.ncbi.nlm.nih.gov/pubmed/17220403

*"These data support the hypothesis that **AZT-induced mitochondrial cardiotoxicity** may be caused by a limiting pool of TTP that lowers mitochondrial DNA replication."*

Blocking of ganglioside synthesis. Gangliosides play an important role in the communication between cells:

- Yan et al. "*3'-Azidothymidine (Zidovudine) Inhibits Glycosylation and Dramatically Alters Glycosphingolipid Synthesis in Whole Cells at Clinically Relevant Concentrations*", J Biol Chem. **1995** Sep 29;270(39):22836-41, https://www.ncbi.nlm.nih.gov/pubmed/7559416

*"**AZT treatment dramatically alters the pattern of glycosphingolipid biosynthesis, nearly abolishing ganglioside synthesis at clinically relevant concentrations** (1-5 microM), and suppresses the incorporation of both sialic acid and galactose into proteins."*

Damage to DNA polymerase and DNA primase. These are enzymes that double the DNA in the normal cell division process (mitosis):

- Nickel et al. „*Interactions of Azidothymidine Triphosphate with the Cellular DNA α, β and γ Polymerases and with DNA Primase*", J. Bio. Chem. Vol. 267, No 2 Jan 15, pp. 848-854, **1992** http://www.jbc.org/content/267/2/848.abstract

Other diseases caused by AZT:

Myopathy (muscle weakness, also affects the heart muscle):

- Scruggs, Naylor, "*Mechanisms of Zidovudine-Induced Mitochondrial Toxicity and Myopathy*", Pharmacology **2008**;82(2):83-8, https://www.ncbi.nlm.nih.gov/pubmed/18504416?dopt=Abstract

"The clinical effectiveness of AZT is constrained due to its association with increased adverse effects, such as myopathy. There are numerous potential mechanisms that may contribute to AZT-induced myopathy."

*"These mechanisms include **AZT-induced oxidative stress**, direct inhibition of mitochondrial bioenergetic machinery, and mitochondrial depletion of L-carnitine. Furthermore, we hypothesize that apoptosis may play a role in AZT-induced myopathy."*

Liver damage (see below, AIDS deaths in France, only 25% die of AIDS-defining diseases, 10 -15% of liver damage):

- Butanda-Ochoa et al. „*A Single Zidovudine (AZT) Administration Delays Hepatic Cell Proliferation by Altering Oxidative State in the Regenerating Rat Liver*", Oxidative Medicine and Cellular Longevity Vol. **2017**, https://www.hindawi.com/journals/omcl/2017/8356175/

*"The results indicate that **AZT significantly decreased DNA synthesis** and the number of mitosis in liver subjected to PH in a synchronized way with the promotion of organelle-selective lipid peroxidation events (especially those observed in plasma membrane and cytosolic fractions) and with liver enzyme release to the bloodstream. Then **at the dose used in clinical practice AZT decreased liver regeneration but stimulates oxidative events** involved during the proliferation process in a way that each membrane system inside the cell preserves its integrity in order to maintain the cell proliferative process."*

Dementia:

- Demir et al. „*Neurotoxic effects of AZT on developing and adult neurogenesis*", Front. Neurosci., 20 March **2015**, ; 9: 93, https://www.frontiersin.org/articles/10.3389/fnins.2015.00093/full

In Demir et al. it becomes clear that it is difficult to distinguish the consequences of AZT from the suspected effects of the HI virus:

„***These data reveal novel negative effects of AZT on neural stem cell biology***. *Given that the sequelae of HIV infection often include neurologic deficits—subsumed under AIDS Dementia Complex (Brew, 1999)—it is important to determine to what extent AZT negatively affects neurological function in ways that contribute to, or exacerbate, ADC in order to avoid attributing iatrogenic drug effects to the underlying disease process, and thereby skewing the risk/benefit analysis of AZT therapy*."

- Caron et al. „*Contribution of mitochondrial dysfunction and oxidative stress to cellular premature senescence induced by antiretroviral thymidine analogues*.", Antivir Ther. **2008**;13(1):27-38, https://www.ncbi.nlm.nih.gov/pubmed/18389896

"Mitochondrial changes and oxidative damage could partly explain the premature senescence of fibroblasts and adipose cells induced by stavudine and zidovudine. ***This suggests that thymidine analogues might be involved in the early aging-related diseases observed in some HIV-infected patients taking antiretroviral drugs.****"*

- Jones et al. "*Assessment of adipokine expression and mitochondrial toxicity in HIV patients with lipoatrophy on stavudine- and zidovudine-containing regimens*.", J Acquir Immune Defic Syndr. **2005** Dec 15;40(5):565-72, https://www.ncbi.nlm.nih.gov/pubmed/16284533

"Patients with LA on d4T-based regimens show evidence of mitochondrial respiratory chain dysfunction, whereas the d4T- and ZDV-based regimens also demonstrated reduced SREBP1c and adiponectin levels, findings that have previously been shown with PIs."

- Schmitz, "Side effects of AZT prophylaxis after occupational exposure to HIV-infected blood.", Ann Hematol. **1994** Sep; 69(3):135-8., https://www.ncbi.nlm.nih.gov/pubmed/8086508

"*The study population comprised health care workers who were taking AZT prophylaxis after accidental exposure to HIV-infected blood. Fourteen individuals were included into the study; seven of them discontinued treatment prematurely, five due to severe subjective symptoms. In case of one worker AZT had to be stopped due to severe neutropenia (800 cells/microliters) with signs of upper respiratory tract infection. Four of 11 individuals taking AZT for at least 4 weeks developed neutropenia (2 WHO I, 1 WHO II, 1 WHO III)."*

"The data presented herein show that AZT causes considerable side effects which must be weighed against the potential protective antiviral effect."

Toxicity of other nucleoside analogs, among others severe liver damage:

There are numerous other examples of the side effects of nucleoside analogs and integrase or protease inhibitors used in HAART therapy, cf.

- Christensen et al. "*Abacavir/Dolutegravir/Lamivudine (Triumeq)–Induced Liver Toxicity in a Human Immunodeficiency Virus–Infected Patient*", Open Forum Infect Dis. **2017** Jun 12;4(3) https://www.ncbi.nlm.nih.gov/pubmed/28748198

- Haas et al. "*Abacavir-induced fulminant hepatic failure in a HIV/HCV co-infected patient*", BMJ Case Rep **2015**, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4680310/

"We report the case of a 50-year-old Caucasian woman with a history significant for HIV, hepatitis C virus and a HLA-B5701+ status, transferred to our emergency department in a hypotensive state and found to have ***acute liver failure, acute renal failure*** *and significant* ***rhabdomyolysis*** *following a change of highly active antiretroviral therapy regimen.*"

"Three weeks prior to admission, the patient had been switched to Triumeq (abacavir/dolutegravir/ lamivudine) for once daily medication dosing. ***Two weeks after switching****, the patient began to develop progressive episodes of nausea, vomiting, diarrhoea, diffuse myalgia and near-syncope."*

- Di Filippo et al. "*Abacavir-induced liver toxicity in an HIV-infected patient*", AIDS **2014**, 28:613–617 https://www.ncbi.nlm.nih.gov/pubmed/24469001

- Pezzani et al. "*Abacavir-induced liver toxicity*", Braz J Infect Dis **2016** , 20(5):502–504 https://www.sciencedirect.com/science/article/pii/S1413867016300435?via%3Dihub

- Calmy et al., "*Low bone mineral density, renal dysfunction, and fracture risk in HIV infection: a cross-sectional study.*", J Infect Dis. **2009** Dec 1;200(11):1746-54, https://www.ncbi.nlm.nih.gov/pubmed/19874178

"*In this mostly male population, low BMD was significantly associated with PI therapy. Tenofovir recipients showed evidence of increased bone turnover."*

- Mallon et al., "*In vivo, nucleoside reverse-transcriptase inhibitors alter expression of both mitochondrial and lipid metabolism genes in the absence of depletion of mitochondrial DNA*.", J Infect Dis. **2005** May 15;191(10):1686-96, https://www.ncbi.nlm.nih.gov/pubmed/15838796

"***Independent of HIV, NRTIs decrease transcription of mtRNA in vivo****."*

- Payne et al., "*Mitochondrial aging is accelerated by anti-retroviral therapy through the clonal expansion of mtDNA mutations.*", Nat Genet. **2011** Jun 26;43(8):806-10, https://www.ncbi.nlm.nih.gov/pubmed/21706004

"*Here we show that patients treated with commonly used nucleoside analog anti-retroviral drugs progressively accumulate somatic mitochondrial DNA (mtDNA) mutations,* ***mirroring those seen much later in life caused by normal aging.****"*

- Fenaux et al. "*Antiviral Nucleotide Incorporation by Recombinant Human Mitochondrial RNA Polymerase Is Predictive of Increased In Vivo Mitochondrial Toxicity Risk*.", Antimicrob Agents Chemother. **2016** Nov 21;60(12): 7077-7085, https://www.ncbi.nlm.nih.gov/pubmed/27645237

"*This study shows **that even moderate levels of nucleotide analog incorporation by POLRMT increase the risk of in vivo mitochondrial dysfunction**. Based on these results, further development of compound 1 as an anti-HCV compound was terminated.*"

- Schweinsburg et al., *"Brain mitochondrial injury in human immunodeficiency virus-seropositive (HIV+) individuals taking nucleoside reverse transcriptase inhibitors."* J Neurovirol. **2005** Aug;11(4):356-64, https://www.ncbi.nlm.nih.gov/pubmed/16206458

*"However, because NRTIs can injure mitochondria, we propose that the observed reductions in NAA in individuals taking didanosine and/or stavudine **may be the result of depleted brain mitochondria and/or alterations in cellular respiration.**"*

- Stauch et al., "*Central nervous system-penetrating antiretrovirals impair energetic reserve in striatal nerve terminals.*", J Neurovirol. **2017** Dec;23(6):795-807, https://www.ncbi.nlm.nih.gov/pubmed/28895059

"*While cortical nerve terminal bioenergetics were not altered, striatal nerve terminals exposed to efavirenz, nevirapine, abacavir, emtricitabine, zidovudine, darunavir, lopinavir, raltegravir, or maraviroc (but not indinavir) exhibit **reduced mitochondrial spare respiratory capacity (SRC).** Further examination of efavirenz and maraviroc revealed a concentration-dependent impairment of striatal nerve terminal maximal mitochondrial respiration and SRC as well as a reduction of intraterminal ATP levels. Depletion of ATP at the synapse may underlie its dysfunction and **contribute to neuronal dysfunction in treated HIV infection**."*

- Kakuda et al. "*Pharmacology of nucleoside and nucleotide reverse transcriptase inhibitor-induced mitochondrial toxicity*.", Clin Ther. **2000** Jun;22(6):685-708, https://www.ncbi.nlm.nih.gov/pubmed/?term=10929917

"The clinical manifestations of NRTI-induced mitochondrial toxicity resemble those of inherited mitochondrial diseases (ie. hepatic steatosis, lactic acidosis, myopathy, nephrotoxicity, peripheral neuropathy, and pancreatitis). Fat redistribution syndrome, or HIV-associated lipodystrophy, is another side effect attributed in part to NRTI therapy. The morphologic and metabolic complications of this syndrome are similar to those of the mitochondrial disorder known as multiple symmetric lipomatosis, suggesting that this too may be related to mitochondrial toxicity. The pathophysiology of less common adverse effects of nucleoside analogue therapy, such as diabetes, ototoxicity, and retinal lesions, may be related to mitochondrial dysfunction but have not been adequately studied."

- Moyle et al. "*Clinical manifestations and management of antiretroviral nucleoside analog-related mitochondrial toxicity*.", Clin Ther. **2000** Aug;22(8):911-36, https://www.ncbi.nlm.nih.gov/pubmed/10972629

*"Depletion of mitochondrial DNA during chronic NRTI therapy may lead to cellular respiratory dysfunction and generalized and tissue- and drug-specific toxicities, including **myopathy**, **peripheral neuropathy**, and*

***lactic acidosis**. Recently, it has been proposed that the fat redistribution syndrome, or lipodystrophy, reported during chronic antiretroviral therapy is a manifestation of the differential impact of at least some NRTIs on peripheral and visceral adipocytes. Management of potential mitochondrial toxicity during NRTI therapy remains a challenge."*

- Chawre et al., "*Zidovudine-induced nail pigmentation in a 12-year-old boy*.", Indian J Pharmacol. **2012** Nov-Dec;44(6):801-2, https://www.ncbi.nlm.nih.gov/pubmed/23248416

*"Zidovudine is an important component of first-line antiretroviral treatment (ART) regimens used to manage pediatric HIV. **Nail pigmentation with zidovudine is a well-documented occurrence in adults**, especially dark-skinned individuals. But it has so far not been reported in children. Here, we report a pediatric case of zidovudine-induced nail pigmentation. A 12-year-old boy receiving ART with zidovudine, lamivudine, and nevirapine presented to dermatology OPD with complaint of diffuse bluish-brown discoloration of all fingernails."*

- Lin et al., "*Risk of diabetes mellitus [DM] in HIV-infected patients receiving highly active antiretroviral therapy: A nationwide population-based study*.", Medicine (Baltimore). **2018** Sep;97(36):e12268 https://www.ncbi.nlm.nih.gov/pubmed/30200166

*"In this nationwide population-based study by including all HIV-infected patients in Taiwan, we found that **exposure to HAART was associated with an increased risk of DM** among HIV-infected patients, particularly in those patients **without** pre-existing hypertension, gout, or HCV infection."*

"Our HIV-infected individuals were observed to have a comparable DM incidence to the general population in similar age groups."

*"Our study found that **HAART, which mainly consisted of 2 NRTIs plus nNRTI or PIs during the study period, was an independent risk factor for DM**. PIs can induce insulin resistance through the inhibition of glucose transporter type 4. **Moreover, NRTIs have been known to cause mitochondrial dysfunction in adipocytes and contribute to lipoatrophy and insulin resistance**."*

*"Our study revealed that HAART was associated with an increased risk of DM, but only in patients **without** comorbidities of hypertension, gout, or HCV infection."*

Toxicity of Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs):

- Hitti et al., "*Maternal toxicity with continuous nevirapine in pregnancy: results from PACTG 1022.*", J Acquir Immune Defic Syndr. **2004** Jul 1;36(3):772-6, https://www.ncbi.nlm.nih.gov/pubmed/15213559

"The study was suspended because of greater than expected toxicity and changes in nevirapine prescribing information."

"*Toxicity was seen in 1 (5%) of 21 subjects randomized to nelfinavir and 5 (29%) of 17 subjects randomized to nevirapine (P = 0.07). **Within the nevirapine group, 1 subject developed fulminant hepatic failure and died, and another developed Stevens-Johnson syndrome**."*

"Continuous nevirapine may be associated with increased toxicity among HIV-1-infected pregnant women with CD4 cell counts greater than 250 cells/microL, as has been observed in non-pregnant women."

- Bertrand et al. "*Antiretroviral Treatment with Efavirenz Disrupts the Blood-Brain Barrier Integrity and Increases Stroke Severity*.", Sci Rep. **2016** Dec 23;6:39738, https://www.ncbi.nlm.nih.gov/pubmed/28008980

"Importantly, Efavirenz exposure increased the severity of stroke in a model of middle cerebral artery occlusion in mice. Taken together, these results indicate that ***selected ARVd can exacerbate HIV-associated cerebrovascular pathology.*** *Therefore, careful consideration should be taken when choosing an anti-retroviral therapy regimen"*

- Taiwo et al., "*Nevirapine toxicity*.", Int J STD AIDS. **2006** Jun;17(6):364-9; https://www.ncbi.nlm.nih.gov/pubmed/16734954

"These toxicities are more common with nevirapine than with efavirenz. Women with CD4 counts >250 cells/mm^3 have particularly increased susceptibility to nevirapine toxicity."

As we will see below, the CD4 cell count has almost no diagnostic value.

- Sastry et al., "*Nevirapine-induced liver lipid-SER inclusions and other ultrastructural aberrations*.", Ultrastruct Pathol. **2018** Mar-Apr;42(2):108-115, https://www.ncbi.nlm.nih.gov/pubmed/29424579

"Nevirapine (NVP) therapy is associated with a high risk of serious liver injury and skin rash. Treatment of Brown Norway rats with NVP causes an immune-mediated skin rash."

*"****In vivo,*** *debris from necrotic hepatocytes and endothelial cells were present in the liver sinusoids, a condition that can trigger an immune response. In addition to* ***mitochondrial, hepatocytic, and endothelial damage, the drug induced large hepatocytic inclusions*** *composed of lipid droplets surrounded by concentric whorls of smooth endoplasmic reticulum (SER) cisternae-lipid-SER (LSER) inclusions, which were deposited in the sinusoids."*

- Paemanee et al., "*Nevirapine induced mitochondrial dysfunction in HepG2 cells.*", Sci Rep. **2017** Aug 23;7(1):9194, https://www.ncbi.nlm.nih.gov/pubmed/28835669

"Mitochondrial dysfunction was observed in response to treatment even with slightly sub-optimal therapeutic treatment concentrations of NVP. This study shows that NVP induces mitochondrial dysregulation in HepG2 cells."

- Tseng et al., "*Incidence and risk factors of skin rashes and hepatotoxicity in HIV-infected patients receiving nevirapine-containing combination antiretroviral therapy in Taiwan*.", Int J Infect Dis. **2014** Dec;29:12-7, https://www.ncbi.nlm.nih.gov/pubmed/25312984

"The incidence of rashes was 21.6% and of hepatotoxicity was 25.5%."

*"****Abnormal liver function at baseline was significantly associated with skin rashes****, while a higher CD4 count and the concurrent use of trimethoprim/sulfamethoxazole were associated with hepatotoxicity after the initiation of nevirapine-containing cART in HIV-infected Taiwanese patients."*

- Mukherjee et al., "*Adverse drug reaction monitoring in patients on antiretroviral therapy in a tertiary care hospital in Eastern India.",* Indian J Pharmacol. **2017** May-Jun;49(3):223-228, https://www.ncbi.nlm.nih.gov/pubmed/29033481

"*32.45% patients of total study participants presented with a total of 330 ADRs [adverse drug reactions]. **Patients from zidovudine-based regimens presented with majority of ADRs such as anemia (up to 36%), central nervous system (CNS), and gastrointestinal (GI) side effects**. Tenofovir-based regimens were, however, found to be mildly safer. **The combination with Efavirenz was associated with majorly CNS side effects while that of nevirapine was associated with rash and pigmentation of nails**. Atazanavir boosted second-line regimens were notably associated with increased serum lipid levels followed by other GI and CNS adverse effects. Increased liver enzymes were found in atazanavir-based second-line ART."*

- Nakku et al., "*HIV status and hearing loss among children between 6 and 12 years of age at a large urban health facility in south western Uganda.*", Int J Pediatr Otorhinolaryngol. **2017** Oct;101:172-177, https://www.ncbi.nlm.nih.gov/pubmed/28964291

*"Prevalence of HL is similar among HIV positive and negative children. Older age of the child, previous ear infection, use of TB drugs and **long duration on ART among the HIV positive children increase the odds of having hearing loss among children.**"*

- Birbal et al. "*Adverse drug reactions associated with antiretroviral therapy in South Africa*.", Afr J AIDS Res. **2016** Sep;15(3):243-8. https://www.ncbi.nlm.nih.gov/pubmed/27681148

*"Female patients were more likely to experience **peripheral neuropathy, lipodystrophy, skin rash, anaemia and hyperlactatemia**, while male patients were more prone to experience **gynaecomastia and peripheral neuropathy**. In addition, patients aged 30-44 years reported the most ADRs. **Most reactions resulted from the use of stavudine, efavirenz, zidovudine, nevirapine and tenofovi**r in the population groups identified in this study."*

Another component besides HAART's nucleoside analogues are integrase inhibitors (INSTI) or protease inhibitors (PI). These substances are said to inhibit enzymes produced by retroviruses. Unfortunately, they are not only doing that.

Toxicity of integrase inhibitors (INI) and protease inhibitors (PI):

- Harris et al. "*Exacerbation of depression associated with starting raltegravir: a report of four cases*", AIDS, **2008**, Vol 22 (14), p. 1890–1892, https://journals.lww.com/aidsonline/FullText/2008/09120/Exacerbation_of_depression_associated_with.30.aspx

- Kheloufi et al., "*Psychiatric disorders after starting dolutegravir: report of four cases*.", AIDS. **2015** Aug 24;29(13):1723-5, https://www.ncbi.nlm.nih.gov/pubmed/26372287

- de Boer et al. "*Intolerance of dolutegravir-containing combination antiretroviral therapy regimens in real-life clinical practice.*", AIDS **2016**, 30(18), p. 2831-2834, https://www.ncbi.nlm.nih.gov/pubmed/27824625

*"**Overall, in 85 patients (15.3%), DGV was stopped.** In 76 patients (13.7%), this was due to intolerability. Insomnia and sleep disturbance (5.6%), gastrointestinal complaints (4.3%) and neuropsychiatric symptoms such as anxiety, psychosis and depression (4.3%) were the predominant reasons for switching DGV."*

- **Termination of the study:**

Brooks et al. "*Cytokine-Mediated Systemic Adverse Drug Reactions in a Drug–Drug Interaction Study of Dolutegravir With Once-Weekly Isoniazid and Rifapentine*", Clin Infect Dis, Vol 67(2), **2018**, p. 193–201, https://academic.oup.com/cid/article/67/2/193/4836314

- Santoriello et al., „*Atazanavir-Associated Crystalline Nephropathy*.", Am J Kidney Dis. **2017** Oct;70(4):576-580, https://www.ncbi.nlm.nih.gov/pubmed/28579422

*"Kidney biopsy revealed a crystalline nephropathy associated with diffuse chronic and granulomatous interstitial inflammation. Following the biopsy, **treatment with ATV was discontinued and kidney function returned to pretreatment baseline levels.**"*

- Hirakawa et al., "*Antiretroviral Therapy Containing HIV Protease Inhibitors Enhances Fracture Risk by Impairing Osteoblast Differentiation and Bone Quality.*", J Infect Dis. **2017** Jun 15;215(12):1893-1897, https://www.ncbi.nlm.nih.gov/pubmed/28525596

*"The results demonstrated significantly higher undercarboxylated osteocalcin and pentosidine in PI-treated patients. Switching to integrase strand transfer inhibitor significant decreased these markers. We also showed impaired bone mechanical properties with higher undercarboxylated osteocalcin level in PI-treated mice and inhibited osteoblast differentiation in PI-treated osteogenic cells. **The results confirmed the adverse effects of PIs on bone quality and osteoblast differentiation.**"*

- Muhammad et al., "*Metabolic syndrome among HIV infected patients: A comparative cross sectional study in northwestern Nigeria*.", Diabetes Metab Syndr. **2017** Nov;11 Suppl 1:S523-S529, https://www.ncbi.nlm.nih.gov/pubmed/28410829

*"**Exposure to HAART particularly protease inhibitor based regimen increases the risk of MS among HIV-infected patients.**"*

- Ascher et al. "*Indinavir Sulfate Renal Toxicity in a Pediatric Hemophiliac with HIV Infection*", Annals of Pharmacotherapy Vol 31, Issue 10, pp. 1146 – 1149, October 1, **1997**, http://journals.sagepub.com/doi/abs/10.1177/106002809703101005

"*The patient developed gross hematuria, proteinuria, pyuria, abdominal pain, increased bilirubin, an elevated serum creatinine (SCr) of 1.2 mg/dL (baseline 0.9–1.0), and* ***symptoms of renal colic within 1 month of starting indinavir sulfate therapy.****"*

- Pat Rolands, "*My Adventures with Crixivan or Toxic Side Effects, Anyone?*", **1997**, http://www.thebody.com/content/art332.html

"*The 'side-effect' I suffered from this drug was complete blockage of my left kidney,* ***almost causing kidney failure.****"*

- McLaughlin et al., "*Renal effects of non-tenofovir antiretroviral therapy in patients living with HIV*.", Drugs Context. **2018** Mar 21;7:212519, https://www.ncbi.nlm.nih.gov/pubmed/29623097

"The literature involving ***renal adverse effects*** *and antiretroviral therapy is most robust with protease inhibitors, specifically atazanavir and indinavir, and includes reports of crystalluria, leukocyturia, nephritis, nephrolithiasis, nephropathy and urolithiasis. Several case reports describe potential nephropathy (including Fanconi syndrome) secondary to administration of abacavir, didanosine, lamivudine and stavudine."*

- Loens et al., "*Nephrotoxicity of antiretrovirals other than tenofovir*", Nephrol Ther. **2018** Feb; 14(1):55-66, https://www.ncbi.nlm.nih.gov/pubmed/29500080

"However, this side effect is not due to a direct dysfunction of the kidneys. Zalcitabine was withdrawn from the market because of this risk. Indinavir, a protease inhibitor, is soluble only in very acidic solutions. Consequently, the small fraction that is excreted in the urine precipitates and ***can be responsible for uro-nephrolithiasis, leukocyturia, cristalluria, obstructive acute kidney failure, and acute or chronic interstitial nephritis.****"*

- Ganta, Chaubey, "*Endoplasmic reticulum stress leads to mitochondria-mediated apoptosis in cells treated with anti-HIV protease inhibitor ritonavir*.", Cell Biol Toxicol. **2019** Jun;35(3):189-204, https://www.ncbi.nlm.nih.gov/pubmed/30386960

"The ***cytotoxic effects of ritonavir involved the interplay of ER stress and mitochondria-mediated apoptosis****."*

- McMahon et al., "*High rates of incident diabetes and prediabetes are evident in men with treated HIV followed for 11 years.*", AIDS. **2018** Feb 20;32(4):451-459, https://www.ncbi.nlm.nih.gov/pubmed/29381559

"In a subgroup who underwent further oral glucose tolerance testing, ***60% had a glucose disorder****, the majority not detected by fasting glucose."*

"*Men with long-term treated HIV infection have high rates of incident glucose disorders associated with modest abdominal fat gain.*"

- Friis-Møller et al., "*Cardiovascular disease risk factors in HIV patients--association with antiretroviral therapy. Results from the DAD study.*", AIDS. **2003** May 23;17(8):1179-93, https://www.ncbi.nlm.nih.gov/pubmed/12819520

"Of specific concern is the fact that use of the NNRTI and PI drug classes (alone and especially in combination), ***particularly among older subjects with normalized CD4 cell counts and suppressed HIV replication, was associated with a lipid profile known to increase the risk of coronary heart disease****."*

- Wand et al. "*Metabolic syndrome, cardiovascular disease and type 2 diabetes mellitus after initiation of antiretroviral therapy in HIV infection*.", AIDS. **2007** Nov 30;21(18):2445-53, https://www.ncbi.nlm.nih.gov/pubmed/18025881

"*Substantial progression to MS [Metabolic syndrome] occurs* ***within 3 years following initiation of ART****.*"

- Ekoru et al. „*HIV treatment is associated with a two-fold higher probability of raised triglycerides: Pooled Analyses in 21 023 individuals in sub-Saharan Africa*.", Glob Health Epidemiol Genom. **2018**;3, https://www.ncbi.nlm.nih.gov/pubmed/29881632

"***Evidence from this study confirms the association of ART with raised TG in SSA populations***."

- Carr et al., "*A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors*.", AIDS. **1998** May 7;12(7):F51-8, https://www.ncbi.nlm.nih.gov/pubmed/9619798

Lipodystrophy was observed clinically in 74 (64%) protease inhibitor recipients after a mean 13.9 months *and 1(3%) protease inhibitor-naive patient (P=0.0001). Fat loss occurred in all regions except the abdomen after a median 10 months.* ***Patients with lipodystrophy experienced a relative weight loss of 0.5 kg per month and had significantly higher triglyceride, cholesterol, insulin and C-peptide levels and were more insulin-resistant than protease inhibitor recipients without lipodystrophy****. Patients receiving ritonavir and saquinavir in combination had significantly lower body fat****, higher lipids and shorter time to lipodystrophy than patients receiving indinavir.* ***Three (2%) patients developed new or worsening diabetes mellitus****.*

Weight loss is AIDS-defining.

- Nishana et al., "*HIV integrase inhibitor, Elvitegravir, impairs RAG functions and inhibits V(D)J recombination*", Cell Death and Disease (**2017**) 8, e2852; https://www.nature.com/articles/cddis2017237.pdf

"Importantly, treatment with ***Elvitegravir resulted in significant reduction of mature B lymphocytes in 70%*** *of mice studied."*

*"Thus, our study **suggests a potential risk associated with the use of Elvitegravir** as an antiretroviral drug, considering the evolutionary and **structural similarities between HIV integrase and RAGs**."*

Meanwhile, the question is asked (as of 2017) whether Africa can continue to tolerate this form of therapy, cf.

- Nansseu et al., "*Antiretroviral therapy related adverse effects: Can sub-Saharan Africa cope with the new "test and treat" policy of the World Health Organization*?", Infect Dis Poverty. **2017** Feb 15;6(1):24, https://www.ncbi.nlm.nih.gov/pubmed/28196511

*"The introduction and widespread use of ART have drastically changed the natural history of HIV/AIDS, but exposure to **ART leads to serious medication-related adverse effects mainly explained by mitochondrial toxicities, and the situation will get worse in the near future**. Indeed, ART is associated with an increased risk of developing **cardiovascular disease**, **lipodystrophy**, **prediabetes** and **overt diabetes**, **insulin resistance** and **hyperlactatemia/lactic acidosis.** The prevalence of these disorders is already high in SSA, and the situation will be exacerbated by the implementation of the new WHO recommendations."*

- Tsai et al. "*Effect of antiretroviral therapy use and adherence on the risk of hyperlipidemia among HIV-infected patients, in the highly active antiretroviral therapy era.*", Oncotarget. **2017** Nov 15;8(63):106369-106381, https://www.ncbi.nlm.nih.gov/pubmed/29290955

*"The matched hyperlipidemia group had a larger number of patients using ART and a higher incidence of comorbidities, specifically, respiratory disease and diabetes. **Patients with high ART dosage and dose-dependent manner adherence, respectively, demonstrated an increased risk of hyperlipidemia**. For single ART regimens, **patients receiving nucleoside reverse-transcriptase inhibitors (NRTI/NRTI)- containing regimen had the highest hyperlipidemia risk, followed by protease inhibitor (PI)- containing and non-NRTI-containing regimens.**"*

- Torres, Lewis. "*Aging and HIV/AIDS: pathogenetic role of therapeutic side effects*.", Lab Invest. **2014** Feb;94(2):120-8, Epub 2013 Dec 16, https://www.ncbi.nlm.nih.gov/pubmed/24336070

*"**Antiretroviral therapy has been shown to enhance events seen in biological aging.** Specifically, antiretroviral NRTIs cause mitochondrial dysfunction, oxidative stress, and mitochondrial DNA defects that resemble features of both HANA and aging. **More recent clinical evidence points to telomere shortening caused by NRTI triphosphate-induced inhibition of telomerase, suggesting telomerase reverse transcriptase (TERT) inhibition as being a pathogenetic contributor to premature aging in HIV/AIDS.** PIs may also have a role in premature aging in HIV/AIDS as they cause prelamin A accumulation. Overall, toxic side effects of HAART may both resemble and promote events of aging and are worthy of mechanistic studies."*

- Sutton et al., "*Risk of acute kidney injury in patients with HIV receiving proton pump inhibitors*.", J Comp Eff Res. **2019** Jun 6, https://www.ncbi.nlm.nih.gov/pubmed/31167563

"Results: A total of 21,643 patients (6000 PPI and 15,643 non-PPI) met all study criteria. ***The PPI cohort had twice the risk of AKI compared with controls*** *(2.12, hazard ratio: 1.46-3.1).*

Conclusion: A nationwide cohort study supported the relationship of an increased risk of AKI in patients receiving PPIs."

Sometimes, very rarely, the serious side effects find their way into the daily press, cf.

- Der Standard.at, „*Integrase-Inhibitoren - Die potenziellen Nebenwirkungen von HIV-Medikamenten*", 24. Juni **2019**, https://www.derstandard.at/story/2000105217472/die-potenziellen-nebenwirkungen-von-hiv-medikamenten

*„Unsere Studie fordert jedoch eine erhöhte Pharmakovigilanz für eine potenziell schwerwiegende Langzeittoxizität dieser Substanzen" sagt Streeck. "****Angesichts der weit verbreiteten Nutzung von INSTI*** sind *prospektive Studien erforderlich, um die breiteren klinischen Auswirkungen unserer Ergebnisse zu bestimmen.""*

How much time more? And why is this not checked before admission?

- Korencak et al., "*Effect of HIV infection and antiretroviral therapy on immune cellular functions*", JCI Insight. **2019**;4(12):e126675, https://insight.jci.org/articles/view/126675

"These findings indicate that EVG and DLG use is associated with slow proliferation and impaired respiration with underlying mitochondrial dysfunction, resulting in overall ***decreased cellular function in CD4$^+$ T cells.****"*

A low CD4 cell count is AIDS defining.

Reduction of bone mineral density (BMD) by ART:

- Hoy et al., "*Immediate Initiation of Antiretroviral Therapy for HIV Infection Accelerates Bone Loss Relative to Deferring Therapy: Findings from the START Bone Mineral Density Substudy, a Randomized Trial*.", J Bone Miner Res. **2017** Sep;32(9):1945-1955, https://www.ncbi.nlm.nih.gov/pubmed/28650589

"Through 2.2 years mean follow-up, ***immediate ART resulted in greater BMD declines*** *than deferred ART at the hip (…) and spine (…). BMD declines were greatest in the first year of ART."*

- Carr et al., "*Prevalence of and risk factors for low bone mineral density in untreated HIV infection: a substudy of the INSIGHT Strategic Timing of AntiRetroviral Treatment (START) trial*.", HIV Med. **2015** Apr;16 Suppl 1:137-46, https://www.ncbi.nlm.nih.gov/pubmed/25711332

"In this geographically and racially diverse population of ART-naïve adults with normal CD4 cell counts, low BMD was common, but osteoporosis was rare. ***Lower BMD was significantly associated with traditional risk factors but not with CD4 cell count or viral load****."*

Thus, in untreated HIV+ persons, bone mineral density is dependent on traditional risk factors but not CD4 cell count or PCR viral load. This clearly speaks against the influence of HIV and for the bone-damaging effects of HAART.

- Grund et al., "*Continuous antiretroviral therapy decreases bone mineral density*", AIDS. **2009** Jul 31; 23(12): 1519–1529, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2748675/

"***Continuous ART is associated with decline in BMD*** *and possibly more fractures relative to intermittent, CD4 cell count-guided ART."*

- Tebas et al., "*Accelerated bone mineral loss in HIV-infected patients receiving potent antiretroviral therapy*", AIDS. **2000** Mar 10; 14(4): F63–F67, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3170993/

"Osteopenia and osteoporosis are unique ***metabolic complications associated with protease inhibitor-containing potent antiretroviral regimens****, that appear to be independent of adipose tissue maldistribution."*

- Bernardino et al. "*Bone mineral density and inflammatory and bone biomarkers after darunavir-ritonavir combined with either raltegravir or tenofovir-emtricitabine in antiretroviral-naive adults with HIV-1: a substudy of the NEAT001/ANRS143 randomised trial.*", Lancet HIV. **2015** Nov;2(11):e464-73, https://www.ncbi.nlm.nih.gov/pubmed/26520926

"A raltegravir-based regimen was associated with significantly less loss of bone mineral density than a standard regimen containing tenofovir disoproxil fumarate, and might be a treatment option for patients at high risk of osteopenia or osteoporosis who are not suitable for NtRTIs such as abacavir or tenofovir alafenamide."

- Brown et al. "*Changes in Bone Mineral Density After Initiation of Antiretroviral Treatment With Tenofovir Disoproxil Fumarate/Emtricitabine Plus Atazanavir/Ritonavir, Darunavir/Ritonavir, or Raltegravir.*", J Infect Dis. **2015** Oct 15;212(8):1241-9, https://www.ncbi.nlm.nih.gov/pubmed/25948863

"*BMD losses 96 weeks after ART initiation were similar in magnitude among patients receiving PIs, ATV/r, or DRV/r but lowest among those receiving RAL."*

- Cook et al. "*Bone Mineral Density and Vitamin D Levels in HIV Treatment-Naïve African American Individuals Randomized to Receive HIV Drug Regimens*.", South Med J. **2016** Nov;109(11):712-717, https://www.ncbi.nlm.nih.gov/pubmed/27812717

"Treatment of African American patients with HIV using EFV/FTC/TDF is associated with a reduction in BMD of the hip and sustained reductions of 25(OH)D not seen in the group that received RAL/DRV/r. This phenomenon may have long-term consequences on bone integrity in this population."

- McComsey, et al. "*Bone mineral density and fractures in antiretroviral-naive persons randomized to receive abacavir-lamivudine or tenofovir disoproxil fumarate-emtricitabine along with efavirenz or atazanavir-ritonavir: Aids Clinical Trials Group A5224s, a substudy of ACTG A5202*.", J Infect Dis. **2011** Jun 15;203(12):1791-801, https://www.ncbi.nlm.nih.gov/pubmed/21606537

"Compared with ABC-3TC, TDF-FTC-treated participants had significantly greater decreases in spine and hip BMD, whereas ATV/r led to more significant losses in spine, but not hip, BMD than EFV."

- Assoumou et al., "*Changes in bone mineral density over a 2-year period in HIV-1-infected men under combined antiretroviral therapy with osteopenia.",* AIDS. **2013** Sep 24;27(15):2425-30, https://www.ncbi.nlm.nih.gov/pubmed/24029735

"*Although osteopenia overall modestly changes over 2 years in long-term cART-treated patients,* ***a quarter of patients experienced a significant loss (>1 SDD) associated with TDF exposure****."*

- Gafni et al. "*Tenofovir disoproxil fumarate and an optimized background regimen of antiretroviral agents as salvage therapy: impact on bone mineral density in HIV-infected children*.", Pediatrics. **2006** Sep;118(3):e711-8, https://www.ncbi.nlm.nih.gov/pubmed/16923923

"Two children in whom ***tenofovir disoproxil fumarate was discontinued*** *because of bone loss that exceeded protocol allowances demonstrated partial or complete recovery of bone mineral density by 96 weeks."*

*"****Tenofovir disoproxil fumarate use in children seems to be associated with decreases in bone mineral density that, in some children, stabilize after 24 weeks****. Increases in bone markers and calcium excretion suggest that tenofovir disoproxil fumarate may stimulate bone resorption. Bone turnover is higher in children than in older adolescents and adults because of skeletal growth, potentially explaining the greater effect seen in young children. Decreases in bone mineral density correlate with decreases in viral load and young age,* ***suggesting that young responders may be at greater risk for bone toxicity."***

- Grigsby et al., "*Tenofovir treatment of primary osteoblasts alters gene expression profiles: implications for bone mineral density loss*.", Biochem Biophys Res Commun. **2010** Mar 26;394(1):48-53, https://www.ncbi.nlm.nih.gov/pubmed/20171173

"Strikingly, the changes in gene expression profiles involved in cell signaling, cell cycle and amino acid metabolism, which would likely impact osteoblast function in bone formation. ***Our findings demonstrate for the first time that tenofovir treatment of primary osteoblasts results in gene expression changes that implicate loss of osteoblast function in tenofovir-associated bone mineral density loss.****"*

- Grant et al. "*Tenofovir and bone health*.", Curr Opin HIV AIDS. **2016** May;11(3):326-32, https://www.ncbi.nlm.nih.gov/pubmed/26859637

*"Given these findings**, TDF-containing regimens may be gradually replaced with non-TDF containing regimens** for the treatment of HIV infection, especially in those at higher risk for fragility fracture."*

We still practice. As of **2016**.

- Triant et al. "*Fracture prevalence among human immunodeficiency virus (HIV)-infected versus non-HIV-infected patients in a large U.S. healthcare system*.", J Clin Endocrinol Metab. **2008** Sep;93(9):3499-504, https://www.ncbi.nlm.nih.gov/pubmed/18593764

***"**Whether increased fractures are the sequelae of antiretroviral therapy, increased rates of traditional risk factors such as low weight among HIV-infected patients, or HIV infection, and its accompanying metabolic and inflammatory disturbances, **itself remains to be determined**."*

Most HIV+ "*patients*" were on HAART, cf.

https://www.theaidsreader.com/articles/rapid-hiv-test-has-high-false-positive-rate-risk-fractures-higher-hiv-infected-patients-herpes-drug

*„The prevalence of fracture in the two patient groups was evaluated, and the overall prevalence of bone fractures was 61% higher among the HIV-positive patients. Grinspoon said this proved to be true for men and women, and minority and nonminority patients. **Most of the HIV-infected patients were taking antiretrovirals**. Grinspoon said it remains unknown why the HIV patients were more likely to suffer broken bones. "**Is it the HIV virus? Is it the medicines that are associated with HIV, that patients take for that? Is it some other mechanism? We simply don't know**," he said."*

We simply don't know? – Which standards are applied here to a therapy?

Unfortunately, many drug trials only test different HAART compilations against each other (relative toxicity). This then lacks a relation to the absolute toxicity.

- Gathe et al., "*Patient-Reported Symptoms over 48 Weeks in a Randomized, Open-Label, Phase 3b Non-inferiority Trial of Adults with HIV Switching to Coformulated Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir DF Versus Continuation of Ritonavir-Boosted Protease Inhibitor with Emtricitabine and Tenofovir DF*.", Patient. **2015** Oct;8(5):445-54, https://www.ncbi.nlm.nih.gov/pubmed/26286337

*"At week 4 as compared with baseline, the switch group experienced a statistically significantly lower prevalence in five symptoms (**diarrhea/loose bowels, bloating/pain/gas in stomach, pain/numbness/tingling in hands/feet, nervous/anxious, and trouble remembering**). The lower prevalence of diarrhea/loose bowels, bloating/pain/gas in stomach, and pain/numbness/tingling in hands/feet observed at week 4 was maintained over time. While there were **no significant differences between groups in the prevalence of sad/down/depressed and problems with sex at** week 4 or week 48, longitudinal models indicated the switch group had a statistically significantly decreased prevalence in both symptoms from week 4 to week 48."*

Here another study on the side effects of HAART and on the question of whether HAART ever has an effect other than side effects, cf.

- May et al., "*HIV treatment response and prognosis in Europe and North America in the first decade of highly active antiretroviral therapy: a collaborative analysis.*", Lancet. **2006** Aug 5;368(9534):451-8, https://www.ncbi.nlm.nih.gov/pubmed/16890831

"Virological response after starting HAART improved over calendar years, ***but such improvement has not translated into a decrease in mortality****."*

"The results of this collaborative study, which involved 12 prospective cohorts and over 20 000 patients with HIV-1 from Europe and North America, show that the virological response after starting HAART has improved steadily since 1996. ***However, there was no corresponding decrease in the rates of AIDS, or death, up to 1 year of follow-up.*** *Conversely, there was some evidence for an increase in the rate of AIDS in the most recent period."*

May one speak here of an ineffective therapy?

Further studies on the toxicity of HAART

- Ouattara et al., "*Early upper digestive tract side effects of zidovudine with tenofovir plus emtricitabine in West African adults with high CD4 counts*.", J Int AIDS Soc. **2013**; 16(1): 18059, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3643089/

"We observed an unexpectedly high rate of digestive sAEs in West African adults*, mostly women, who started a 3-nuc ART with TDF/FTC+ZDV in Côte d'Ivoire. These adults were participating in a trial of early ART and had much higher CD4 counts than those who currently routinely start ART in sub-Saharan Africa."*

- Stewart et al., "*Severe antiretroviral-associated skin reactions in South African patients: a case series and case-control analysis*.", Pharmacoepidemiol Drug Saf. **2016** Nov; 25(11):1313-1319, https://www.ncbi.nlm.nih.gov/pubmed/27464823

"We identified 169 severe skin reactions in patients on cART*. The most common presentations were* ***Stevens Johnson syndrome/toxic epidermal necrolysis (49%)*** *and drug hypersensitivity syndrome (36%). One hundred forty-one patients were female, of which* ***27 were pregnant****. Median duration of hospitalization was 12 days (interquartile range 8 to 19)* ***and six patients died."***

Why does medical science call this a *therapy*?

- Suárez-Lorenzo et al., "*Severe reaction to emtricitabine and lamiduvine: evidence of cross-reactivity.*", Contact Dermatitis. **2016** Apr;74(4):253-4, https://www.ncbi.nlm.nih.gov/pubmed/26948418

- Rajesh et al., "*Evaluating the effects of combination antiretroviral therapy regimens and the development of adverse drug reactions in Indian human immunodeficiency virus positive patients*.", Saudi Journal for Health Sciences - Vol 3, Issue 2, May-Aug **2014**, p. 107-117, http://www.saudijhealthsci.org/article.asp?issn=2278-0521;year=2014;volume=3;issue=2;spage=107;epage=117;aulast=Rajesh

*"ADRs were highest with zidovudine + lamivudine + nevirapine (**42.3%**) and tenofovir + emtricitabine + efavirenz (**14.2%**). On bivariate analysis, (P < 0.001) were identified in*
*1) **Anemia** with zidovudine use,*
*2) **Pancytopenia** with zidovudine, lamivudine use*
*3) **Hepatotoxicity** with nevirapine, efavirenz use,*
*4) **Peripheral neuropathy** with stavudine use,*
*5) **Renal failure** with tenofovir use and*
*6) **Maculopapular rash** with emtricitabine, tenofovir, efavirenz use.*

*The system organ class most affected with ADRs to cART was **red blood cell disorders** (**30.9%**) followed by **skin and appendages disorders** (**16.5%**)."*

From here Table 3:

Table 3: Adverse drug reactions characteristics of combination antiretroviral therapy to system organ classes and codes [WHO-ART code]

System organ class [WHO-ART code]; *n* (%) Adverse drug reaction		Number of ADRs (%) (*n*=230)	Suspected antiretroviral medications	*P* value
Red blood cell disorders [1210]; 71 (30.9)				
Anaemia		42 (18.3)	Zidovudine use	<0.001
Grade 1 anemia (9.5-10.5g/dl)	2 (4.8%)			
Grade 2 anemia (8.0-9.4g/dl)	27 (64.2%)			
Grade 3 anemia (6.5-7.9g/dl)	5 (12%)			
Grade 4 anemia (<6.5g/dl)	8 (19%)			
Pancytopenia		22 (10)	Zidovudine, Lamivudine use	<0.001
Hyperbilirubinemia		4 (1.8)	Zidovudine, Atazanavir use	0.080
Marrow depression		2 (0.9)	Zidovudine use	0.153
Eosinophilia		1 (0.4)	Zidovudine use	0.313
Skin and appendages disorders [0100]; 37 (16.5)				
Maculopapular rash		8 (3.4)	Emtricitabine, Tenofovir, Efavirenz use	<0.001
Erythematous rash		7 (3)	Efavirenz/Nevirapine use	0.153
Hyper pigmentations		7 (3)	Zidovudine, Nevirapine use	0.007
SJS		4 (1.8)	Nevirapine use	0.043
Itching/pruritus		3 (1.3)	Zidovudine use	

Drug hypersensitivity syndrome	2 (0.9)	Abacavir use	
Erythrema multiform	2 (0.9)	Nevirapine use	
TEN	2 (0.9)	Nevirapine use	
Exforiative dermatitis	1 (0.4)	Efavirenz use	
Vesiculobullous reactions	1 (0.4)	Emtricitabine use	
Gastro-intestinal system disorders [0600]; 27 (11.7)			
Vomiting	13 (5.7)	Zidovudine use	0.126
Nausea	7 (3)	Zidovudine use	
Diarrhoea	4 (1.7)	Lopinavir/Ritonavir use	
Pancreatitis	3 (1.3)	Lopinavir-Ritonavir use and Stavudine use	
Central and PNS disorders [0410]; 27 (11.7)			
Peripheral neuropathy	15 (6.5)	Stavudine use	<0.001
Headache	4 (1.8)	Emtricitabine, Tenofovir, Efavirenz use	0.013
Dizziness	3 (1.3)	Indinavir use	0.080
Hallucination	1 (0.4)	Efavirenz use	
Depression	1 (0.4)	Efavirenz use	
Giddiness	1 (0.4)	Efavirenz use	
Seizure	1 (0.4)	Lamivudine use	
Confusion	1 (0.4)	Efavirenz use	
Liver and biliary system disorders [0700]; 25 (10.8)			
Hepatotoxicity	19 (8.2)	Nevirapine, Efavirenz use	<0.001
Fatty liver	4 (1.8)	Stavudine, zidovudine use	
Hepatitis	3 (1.3)	Nevirapine use	
Urinary system disorders [1300]; 12 (5.2)			
Renal failure	9 (3.7)	Tenofovir+Emtricitabine+Efavirenz, Tenofovir+Lamivudine+Efavirenz	<0.001
Nephrolithiasis	2 (0.9)	Indinavir use	
White cell and RES disorders [1220]; 11 (4.8)			
Leucopenia	8 (3.4)	Zidovudine, lamivudine use	<0.001
Neutropenia	3 (1.3)	Zidovudine, lamivudine use	0.043
Body as a whole, general disorders [1810]; 7 (3)			
Fever	4 (1.8)	Zidovudine, lamivudine use	
Pedal edema	3 (1.3)	Stavudine use	
Psychiatric disorders [0500]; 5 (2.1)			
Sleep disorder	3 (1.3)	Efavirenz use	
Excitability	2 (0.9)	Efavirenz use	
Metabolic and nutritional disorders [0800]; 5 (2.1)			
Lipodystrophy	2 (0.9)	Stavudine use	
Lactoacidosis	1 (0.4)	Zidovudine use	
Dyslipidemia	2 (0.9)	Nevirapine use	
Musculo-skeletal system disorders [0200]; 1 (0.4)			
Myopathy/Weakness	1 (0.4)	Zidovudine use	
Vascular (extra cardiac) disorders [1040]; 1 (0.4)			
Vacuities	1 (0.4)	Indinavir use	
Resistance mechanism disorders [1830]; 1 (0.4)			
IRIS	1 (0.4)	Tenofovir+Emtricitabine+Efavirenz,	0.080

P value of <0.05 was considered as statistically significant by bivariate analysis. TEN:Toxic epidermal necrolysis, SJS:Steven johnson syndrome, PNS:Peripheral nervous system, IRIS:Immune reconstitution inflammatory syndrome, RES:Reticulo-endothelial system, cART:Combination antiretroviral therapy, ADRs:Adverse drug reactions

- Ndona et al., "*Nadir CD4+, religion, antiretroviral therapy, incidence of type 2 diabetes mellitus, and increasing rates of obesity among black Africans with HIV disease*.", Int J Gen Med. **2012**;5:983-90, https://www.ncbi.nlm.nih.gov/pubmed/23226071

***"ART-related obesity and type 2 diabetes** are becoming increasing problems in Central Africans with HIV disease."*

- Gomes et al., "*Incidence of Diabetes Mellitus and Obesity and the Overlap of Comorbidities in HIV+ Hispanics Initiating Antiretroviral Therapy*.", PLoS One. **2016** Aug 10;11(8):e0160797, https://www.ncbi.nlm.nih.gov/pubmed/27508301

*"In this Hispanic cohort in an LMIC, incidences of IFG/DM and overweight/obesity were similar to or higher than that found in high income countries, and **cardiometabolic disorders affected three-quarters of those initiating ART**."*

- Lewis, "*Defective mitochondrial DNA replication and NRTIs: pathophysiological implications in AIDS cardiomyopathy*.", Am J Physiol Heart Circ Physiol. **2003** Jan;284(1):H1-9, https://www.ncbi.nlm.nih.gov/pubmed/12485813

"*Clinical experience, pharmacological, cellular, and molecular biological evidence links altered mitochondrial DNA (mtDNA) replication to the toxicity of NRTI (8, 56, 57, 67, 68, 115, 132) in many tissues. mtDNA replication defects and mtDNA depletion in target tissues are observed clinically and experimentally. A working hypothesis explains the varied clinical side effects and invokes mitochondrial toxicity from NRTIs in HAART. Organ-specific pathological changes or diverse systemic effects result from and are frequently attributed to HAART, in which NRTIs are included (5, 7, 16, 35,53, 81, 90, 96, 110, 117, 124)."*

- Gardner, "*HIV treatment and associated mitochondrial pathology: review of 25 years of in vitro, animal, and human studies*.", Toxicol Pathol. **2014** Jul;42(5):811-22, https://www.ncbi.nlm.nih.gov/pubmed/24067671

*"In 1988, the suggestion that the first antiretroviral drug, zidovudine, was the potential cause of muscle pathology in HIV-infected persons resulted in structural and biochemical patient studies demonstrating acquired mitochondrial dysfunction. Assessment of subsequent nucleoside analog reverse transcriptase inhibitor (NRTI) antiretroviral drugs has indicated that mitochondria are a common target of **NRTI toxicity in multiple tissues**, leading to a wide variety of pathology ranging from lipodystrophy to neuropathy. **Overwhelmingly, these complications have emerged during post-licensing human studies."***

***"Millions of patients have been treated with mitochondrially toxic NRTIs** and these drugs remain the backbone of antiretroviral rollout in much of sub-Saharan Africa."*

- Science Daily, "*Highly Active Antiretroviral Therapy (HAART) Leads To Pulmonary Hypertension, Study Suggests*", American Journal of Pathology, March 2, **2009**, https://www.sciencedaily.com/releases/2009/02/090223124133.htm

"Researchers have discovered that HAART contributes to pulmonary hypertension in HIV-infected patients."

or

- Wang et al., "*Roles and mechanisms of human immunodeficiency virus protease inhibitor ritonavir and other anti-human immunodeficiency virus drugs in endothelial dysfunction of porcine pulmonary arteries and human pulmonary artery endothelial cells.*", Am J Pathol. **2009** Mar;174(3):771-81, https://www.ncbi.nlm.nih.gov/pubmed/19218343

*"Thus, **HAART drugs significantly impair endothelial functions of porcine pulmonary arteries** and HPAECs, which may be mediated by eNOS down-regulation, oxidative stress, and ERK1/2 activation. These findings suggest that HAART drugs may contribute to the high incidence of pulmonary artery hypertension in human immunodeficiency virus-infected patients."*

- Lin et al., "*Zidovudine-Mediated Autophagy Inhibition Enhances Mitochondrial Toxicity in Muscle Cells*.", Antimicrob Agents Chemother. **2018** Dec 21;63(1), Print **2019** Jan, https://www.ncbi.nlm.nih.gov/pubmed/30373793

*"Nucleoside reverse transcriptase inhibitors (NRTIs), such as zidovudine (AZT), are **part of numerous regimens for the treatment of HIV infection or for the prevention of mother-to-child transmission** (MTCT), particularly in resource-poor HIV/AIDS populations (1). Prolonged NRTI exposure to thymidine analogues has been associated with **mitochondrial toxicities to heart, liver, and skeletal muscle** (2, 3)."*

*"Taken our findings together, our study reveals a novel mechanism of **how thymidine analogues contribute to myodegenerative diseases**. These data also provide evidence for an important role of autophagy in cardiac and skeletal muscle disease in HIV-infected patients."*

- Honnapurmath et al. "*Antiretroviral Therapy-induced Insulin Resistance and Oxidative Deoxy Nucleic Acid Damage in Human Immunodeficiency Virus-1 Patients*.", Indian J Endocrinol Metab. **2017** Mar-Apr;21(2):316-321, https://www.ncbi.nlm.nih.gov/pubmed/28459032

*"All subjects were randomly selected and grouped as HIV-negative (control group) (n = 300), HIV-positive without ART (n = 100), HIV-positive with ART first line (n = 100), and HIV-positive with ART second line (n = 100). **IR and oxidative DNA damage were significantly higher in HIV-positive patients with second-line ART and HIV-positive patients with first-line ART than ART-naive patients**. In a linear regression analysis, increased IR was positively associated with the increased DNA damage (odds ratio: 3.052, 95% confidence interval: 2.595-3.509) P < 0.001."*

- Marbaniang, et al., "*High prevalence of insulin resistance and occurrence prior to hyperinsulinemia threshold among people living with HIV in Pune, India*.", Diabetes Metab Syndr. **2019** May - Jun;13(3):1813-1819, https://www.ncbi.nlm.nih.gov/pubmed/31235099

*"Thirty-five percent were centrally obese, 75% were adherent to WHO recommended physical activity guidelines. Prevalence of diabetes, prediabetes, IR were 9%, 16% and 38%, respectively. Twenty-nine percent non-diabetics had IR and it occurred much prior to the threshold for hyperinsulinemia. **IR was associated with the use of ART drugs** (OR: **6.6**, 95% CI: 2.9-15.2 and **5.4**, 95% CI: 2.2-13.6 for first- and second line ART respectively) and central obesity (OR:1.9, 95% CI: 1.1-3.4)."*

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- Hernández et al., "*Increased incidences of noninfectious comorbidities among aging populations living with human immunodeficiency virus in Ecuador: a multicenter retrospective analysis*.", HIV AIDS (Auckl). **2019** Apr 1;11:55-59, https://www.ncbi.nlm.nih.gov/pubmed/31114389

"The average age at HIV diagnosis was 34.1 years old and cART in average was started 15.9 months after HIV-diagnosis. ***Recruited patients were receiving cART for an average of 59.2±40.2 months. Only 9.9% (n=50) of the patients did not show any NICMs [noninfectious comorbidities]****. Diabetes and pre-diabetes was found in 6% (n=30) and 16.3% (n=82) patients, respectively; however, dyslipidemia and overweight/obesity was frequent, as they affected 41.4% (n=208) and 36.4% (n=183) patients, respectively."*

"*Conclusion****: Prevalence of NICMs among subjects under cART was greater than that reported among the Ecuadorian general population****, therefore specific public health actions are required to make patients aware of and prevent NICMs among PLHIV in Ecuador."*

- Kansiime et al., "*Prevalence of non-communicable diseases among HIV positive patients on antiretroviral therapy at joint clinical research centre, Lubowa, Uganda*.", PLoS One. **2019** Aug 9;14(8):e0221022, https://www.ncbi.nlm.nih.gov/pubmed/31398244

"This was a cross-sectional study conducted among 387 systematically sampled patients, ***receiving ART*** *at the Joint Clinical Research Centre, Lubowa, between March and April 2017."*

"The overall prevalence of having at least one NCD [non-communicable diseases] was 20.7% (…). The prevalence of ***hypertension*** *was 12.4% (…),* ***osteoporosis*** *6.5% (…),* ***diabetes mellitus*** *4.7% (…),* ***renal impairment*** *1.6% (…),* ***asthma*** *1.6% (…), and* ***cardiomyopathy*** *1.3% (…). Prevalence of multi-morbidity was 4.7% (…). Prevalence was significantly higher among older participants, widowed participants and individuals with an opportunistic infection."*

- Mugendi et al., "*Prevalence and Correlates of Neurocognitive Disorders among HIV Patients on Antiretroviral Therapy at a Kenyan Hospital*.", Neurol Res Int. **2019** Oct 30;2019:5173289, https://www.ncbi.nlm.nih.gov/pubmed/31781391

"Mean duration since HIV diagnosis and mean duration on ART were ***6.3*** *(±SD 3.7) and* ***5.6 years*** *(±SD 3.4), respectively. Median CD4 count at interview was 446 cells/mm3 (interquartile range (IQR) 278-596).* ***Eighty-eight percent of participants screened positive for HAND****, of whom 87% had asymptomatic neurocognitive impairment (ANI) and minor neurocognitive disorders (MND) grouped together while 1% had HIV-associated dementia (HAD).* ***Patients on AZT/3TC/EFV were 3.7 times more likely to have HAND (OR = 3.7, p=0.03) compared to other HAART regimens****."*

How many more proves are needed until science accepts how deadly AZT is?

4.1. HAART and pregnancy or children

The serious adverse effects of the drug combinations of HAART (= *ARV*) affect particularly children. Here it must be distinguished between the effects on the fetus, during pregnancy and the effects on the born child.

In HIV+ measured pregnant women, a so-called HIV prophylaxis based on HAART is performed, with the most serious adverse effects for the child.

- Bong et al. "*Risk factors for early mortality in children on adult fixed-dose combination antiretroviral treatment in a central hospital in Malawi*.", AIDS. **2007** Aug 20;21(13):1805-10, https://www.ncbi.nlm.nih.gov/pubmed/17690580

*"**Although children do well on ART, there is high early mortality."***

"*By September 2006, **49 children (11%) had died**, of whom 35 (71%) died by 3 months and 44 (89%) by 6 months. **The cumulative incidence of death at 3, 6, 12 and 24 months after ART was 8, 12, 13 and 15%, respectively."***

- Tooke et al., "*Antiretrovirals causing severe pre-eclampsia*.", Pregnancy Hypertens. **2016** Oct;6(4):266-268, https://www.ncbi.nlm.nih.gov/pubmed/27939465

*"The main indication (59%) for delivery of the infant was hypertension related with the majority of these (94%) being classified as pre-eclampsia. Although HIV on its own showed no association (p=0.13), **mothers who received greater than 4 weeks of antiretrovirals were more likely to develop severe pre-eclampsia** (p=0.007)."*

- Newschaffer et al. "*Prenatal zidovudine use and congenital anomalies in a medicaid population*.", J Acquir Immune Defic Syndr. **2000** Jul 1;24(3):249-56, https://www.ncbi.nlm.nih.gov/pubmed/10969349

"*Children of study women who were prescribed ZDV had **increased adjusted odds of any anomaly**,…*"

- Italian Register Study, "*Rapid disease progression in HIV-1 perinatally infected children born to mothers receiving zidovudine monotherapy during pregnancy. The Italian register for HIV Infection in Children*.", AIDS. **1999** May 28;13(8):927-33, https://www.ncbi.nlm.nih.gov/pubmed/10371173

"*Comparison of HIV-1-infected children whose mothers were treated with ZDV with children whose mothers were not treated **showed that the former group had a higher probability of developing severe disease**,…*"

*"The probability of developing severe disease at 3 years of life (Fig. 2) **was significantly higher in children born to ZDV+ mothers** (57.3%) than in those born to ZDV- mothers (37.2%)."*

- Li et al., "*Antiretroviral Therapy in Relation to Birth Outcomes among HIV-infected Women: A Cohort Study.*", J Infect Dis. **2016** Apr 1;213(7):1057-64, https://www.ncbi.nlm.nih.gov/pubmed/26265780

*"Our findings demonstrate an **increased risk of adverse birth outcomes associated with the use of highly active antiretroviral therapy during pregnancy.**"*

- Donà et al., "*Impact of HIV-1 Infection and Antiretroviral Therapy on Bone Homeostasis and Mineral Density in Vertically Infected Patients*.", J Osteoporos. **2019** Jan 1;2019:1279318, eCollection 2019, https://www.ncbi.nlm.nih.gov/pubmed/30693083

*"**About the impact of HIV infection on BMD, we found no correlation between severe disease (CDC stage B/C) and z-score.**"*

*"**As expected, a significant correlation between ART total duration and z-score (both lumbar and femoral) was described**. In our study, the mean duration of ART in the cohort who underwent DXA is 13,4 years. Even if the impact of ART in the pediatric population is not easy to interpret, considering the wide age range and the interindividual differences in pubertal development, **the negative effect of ART has already been described by other authors**."*

- Manafe et al., "*Need for active cardiovascular screening in HIV-infected children under antiretroviral therapy in Africa.*", Cardiovasc Diagn Ther. **2019** Feb;9(1):68-72, https://www.ncbi.nlm.nih.gov/pubmed/30881881

*"The pathogenesis and long-term outcomes of ART in children are not well understood, but **even in the context of viral suppression there seems to be an increased cardiovascular risk due to metabolic syndrome compared to that of uninfected children** (13,17,18)."*

- García-Otero et al., "*Cardiac and mitochondrial function in HIV-uninfected fetuses exposed to antiretroviral treatment.*", PLoS One. **2019** Mar 4;14(3):e0213279, https://www.ncbi.nlm.nih.gov/pubmed/30830946

*"**HEU fetuses showed signs of increased myocardial and mitochondrial mass associated with maternal zidovudine treatment, suggesting a fetal adaptive response to cART toxicity**."*

*"Indeed, the present study also confirms previous data suggesting a **significant association between fetal myocardial hypertrophy and the use of zidovudine during pregnancy**."*

*"In conclusion, in the present cohort we confirmed the presence of fetal cardiac hypertrophy and further report signs of increased mitochondrial number in HEU fetuses, being **both associated with maternal zidovudine treatment during pregnancy.**"*

The growing heart of the **uninfected fetus** (HEU) attempts to compensate for the severe cytotoxic agents of the mother's antiviral therapy, which pass through the placenta. Later, this leads to severe heart damages.

- Lipshultz et al. "*Cardiac effects of antiretroviral therapy in HIV-negative infants born to HIV-positive mothers: NHLBI CHAART-1 (National Heart, Lung, and Blood Institute Cardiovascular Status of HAART Therapy in HIV-Exposed Infants and Children cohort study)*.", J Am Coll Cardiol. **2011** Jan 4;57(1):76-85, https://www.ncbi.nlm.nih.gov/pubmed/21185505

"In ART+ infants, LV fractional shortening was higher than in ART- infants; girls showed a greater difference."

"CONCLUSIONS: ***Fetal exposure to ART is associated with reduced LV mass, LV dimension, and septal wall thickness z-scores and increased LV fractional shortening and contractility up to age 2 years****. These effects are more pronounced in girls than in boys."*

These children were **HIV negative**. Many publications speak of "*HIV exposed*". Wouldn't it be better to speak of "*HAART exposed*" (= ART+)?

The teratogenic effects of HAART are confirmed in animal experiments, cf.

- Liu et al., "*Mitochondrial compromise in 3-year old patas monkeys exposed in utero to human-equivalent antiretroviral therapies.*", Environ Mol Mutagen. **2016** Aug;57(7):526-34, https://www.ncbi.nlm.nih.gov/pubmed/27452341

"Overall the data show that 3-year-old patas sustain ***persistent mitochondrial dysfunction*** *as a result of perinatal ARV drug exposure."*

- Poirier et al., "*Fetal consequences of maternal antiretroviral nucleoside reverse transcriptase inhibitor use in human and nonhuman primate pregnancy*.", Curr Opin Pediatr. **2015** Apr;27(2):233-9, https://www.ncbi.nlm.nih.gov/pubmed/25635584

"NRTI-exposed patas offspring showed a compensatory increase in heart mtDNA, and ***a 50% loss of brain mtDNA at 1 year of age****. Mitochondrial morphological damage and mtDNA loss were* ***persistent in blood cells of NRTI-exposed infants*** *up to 2 years of age, and in heart and brain from NRTI-exposed patas up to 3 years of age (human equivalent of 15 years)."*

- Poirier et al., "*Perinatal genotoxicity and carcinogenicity of anti-retroviral nucleoside analog drugs*.", Toxicol Appl Pharmacol. **2004** Sep 1;199(2):151-61, https://www.ncbi.nlm.nih.gov/pubmed/15313587

"Studies in rodents have demonstrated AZT-DNA incorporation, ***HPRT mutagenesis****,* ***telomere shortening****, and* ***tumorigenicity*** *in organs of fetal mice exposed transplacentally to AZT. In monkeys, both AZT and 3TC become* ***incorporated into the DNA from multiple fetal organs*** *taken at birth after administration of human-equivalent protocols to pregnant dams during gestation, and telomere shortening has been found in monkey fetuses exposed to both drugs. In human infants, AZT-DNA and 3TC-DNA incorporation as well as* ***HPRT and GPA mutagenesis*** *have been documented in cord blood from infants exposed in utero to Combivir."*

- Lagathu et al., "*Metabolic complications affecting adipose tissue, lipid and glucose metabolism associated with HIV antiretroviral treatment*.", Expert Opin Drug Saf. **2019** Jul 19:1-12, https://www.ncbi.nlm.nih.gov/pubmed/31304808

"Altered fat repartition, diagnosed as lipodystrophy, has been related to first-generation nucleoside-reverse-transcriptase-inhibitors (NRTIs) (stavudine zidovudine) and some protease inhibitors (PIs). Recently, use of some integrase-inhibitors (INSTI) resulted in weight/fat gain, which represents a ***worrisome unresolved situation****. Lipid parameters were affected by some first-generation NRTIs, non-NRTIs (efavirenz) but also PIs*

boosted by ritonavir, with increased total and LDL-cholesterol and triglycerides. Insulin resistance is common associated with abdominal obesity. ***Diabetes incidence, high with first-generation-ART (zidovudine, stavudine, didanosine, indinavir) has declined with contemporary ART close to that of the general population.*** *Metabolic syndrome, a dysmetabolic situation with central obesity and insulin resistance, and liver steatosis are common in PLWH and* ***could indirectly result from ART-associated fat gain and insulin resistance***."

- Dirajlal-Fargo et al., "***HIV-exposed-uninfected*** *infants have increased inflammation and monocyte activation*.", AIDS. **2019** Apr 1;33(5):845-853, https://www.ncbi.nlm.nih.gov/pubmed/30649056

*"**HIV-infected mothers received antiretroviral therapy during pregnancy, <u>their infants received zidovudine prophylaxis</u> and were not breastfed.**"*

*"Compared with HIV-unexposed, HEU infants had a **lower mean gestational age** (38.7 vs. 39.3 weeks) and **weight** (3.1 vs. 3.3 kg); and reached **lower weight** (5.9 vs. 8.5 kg) and **height** (53.6 vs. 68.8 cm) **at 6 months**."*

*"**HIV-exposed [uninfected] infants have heightened inflammation and monocyte activation at birth**, which for some markers persisted to 6 months of life and was not related to maternal inflammatory status. **Inflammation may contribute to the increased HEU infectious morbidity and poor growth**."*

- Sibiude et al., "*In utero exposure to zidovudine and heart anomalies in the ANRS French perinatal cohort and the nested PRIMEVA randomized trial*.", Clin Infect Dis. **2015** Jul 15;61(2):270-80, https://www.ncbi.nlm.nih.gov/pubmed/25838291/

*"This study confirms a **specific association between in utero exposure to ZDV and CHDs, and a long-lasting postnatal myocardial remodeling in girls**. A potential common mechanism, including the involvement of mitochondrial dysfunction, must be explored, and long-term consequences on cardiac function warrant specific attention."*

- Hofer et al., "*In Utero Exposure to Antiretroviral Drugs: Effect on Birth Weight and Growth Among HIV-exposed Uninfected Children in Brazil*.", Pediatr Infect Dis J. **2016** Jan;35(1):71-7, https://www.ncbi.nlm.nih.gov/pubmed/26741583

"In HEU children, early exposure to ARVs was associated with lower WAZ at birth and lower LAZ up to 2 years of life."

4.2. HAART and Cancer

At the same time, **cancer is a thread as a long-term consequence** of HIV / AIDS therapy, cf.

- Borges, "*Combination antiretroviral therapy and cancer risk*", Curr Opin HIV AIDS. **2017** Jan; 12(1): 12–19, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5244841/

"*It is thus difficult to disentangle the direct effect of cART on cancer risk from other factors postulated to play a role in carcinogenesis.*"

- Crum-Cianflone, "*Anal Cancers among HIV-Infected Persons: HAART Is Not Slowing Rising Incidence*", AIDS. **2010** Feb 20; 24(4): 535–543, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3132114/

"*Recent data have shown that **non-AIDS-defining cancers (NADCs) are now more common than the traditional AIDS-defining cancers** (ADCs; Kaposi's sarcoma, non-Hodgkin's lymphoma, invasive cervical carcinoma).*"

"*In our study, duration of HAART use was not significantly associated with a decreased risk of anal cancer. Other research concurs with this finding [10]; **one study even demonstrated that HAART was associated with a higher risk of anal cancer** [11], but it is unclear if this was a true effect of ART on cancer or attributable to population effects.*"

- Piketty et al., "*Marked increase in the incidence of invasive anal cancer among HIV-infected patients despite treatment with combination antiretroviral therapy*.", AIDS. **2008** Jun 19;22(10):1203-11, https://www.ncbi.nlm.nih.gov/pubmed/18525266

"***The incidence of anal cancer has increased among HIV-infected patients in France since 1996**. Although an ascertainment bias cannot be excluded, data indicate that **combination antiretroviral therapy does not prevent anal cancer in these patients**.*"

What does premium HIV researcher Jürgen Rockstroh say? Cf.

- Vogel et al. (Co-Author Jürgen Rockstroh) „*Cancer risk in HIV-infected individuals on HAART is largely attributed to oncogenic infections and state of immunocompetence*.", Eur J Med Res (**2011**) 16: 101-107, https://www.ncbi.nlm.nih.gov/pubmed/21486722

*"In addition to AIDS defining cancers about 20 other types of malignancy, particularly those associated with oncogenic infectious agents, occur more frequently in HIV-infected patients and are **probably** also linked to immunodeficiency."*

A little bit more specific?

*"In the Bonn **HIV cohort individuals had a significantly higher risk for cancer as compared to the normal population with an overall standardized incidence ratio of 4 for women and 6 for men**. The cancer risk varied considerable depending on the type of cancer."*

But:

"*CONCLUSIONS:* ***The risk of cancer in the setting of HIV-infection is reduced by antiretroviral therapy*** *but remains above that of the HIV-uninfected reference population in the case of tumor entities with an underlying infectious etiology* ***irrespective if these tumors have been classified as AIDS-defining*** *or not."*

The beneficial HAART Therapy helps against cancer in HIV infected people, whether AIDS-defining cancer or non-AIDS-defining cancer? Shouldn't we expect a certain difference as a therapeutic result in a clearly defined clinical setting? I have doubts about the objectivity of this gentleman and prefer to trust the studies that see a connection between HAART and cancer.

Cf. also

- Mayor at al., *„AIDS-defining neoplasm prevalence in a cohort of HIV-infected patients, before and after highly active antiretroviral therapy*.", Ethn Dis. **2008** Spring;18(2 Suppl 2):S2-189-94, https://www.ncbi.nlm.nih.gov/pubmed/18646347

"*Our study found a significant reduction of Kaposi sarcoma and AIDS-related lymphoma in the HAART era of the AIDS epidemic.* ***A higher prevalence of non-AIDS-defining lymphomas, prostate carcinoma, and cervical carcinoma was seen in the HAART era.*** *These findings suggest that factors other than severe immunosuppression are involved in the neoplasms' pathogenesis."*

- Bower et al., "*HIV-related lung cancer in the era of highly active antiretroviral therapy*.", AIDS. **2003** Feb 14;17(3):371-5, https://www.ncbi.nlm.nih.gov/pubmed/12556691

"In this study HIV-related ***lung cancer occurred more frequently in the post-HAART era, when compared with the HIV-negative population."***

"In this study HIV-related lung cancer occurred more frequently in the post-HAART era, when compared with the HIV-negative population. ***Unfortunately, the outcome of these patients remains poor despite HAART****."*

- Engels et al., "*Elevated incidence of lung cancer among HIV-infected individuals*.", J Clin Oncol. **2006** Mar 20;24(9):1383-8, https://www.ncbi.nlm.nih.gov/pubmed/16549832

"***Incidence tended to increase with calendar year (P = .09) and HAART use (P = .10)****, and was inversely related to HIV viral load (P = .03), but these associations were attenuated with age adjustment."*

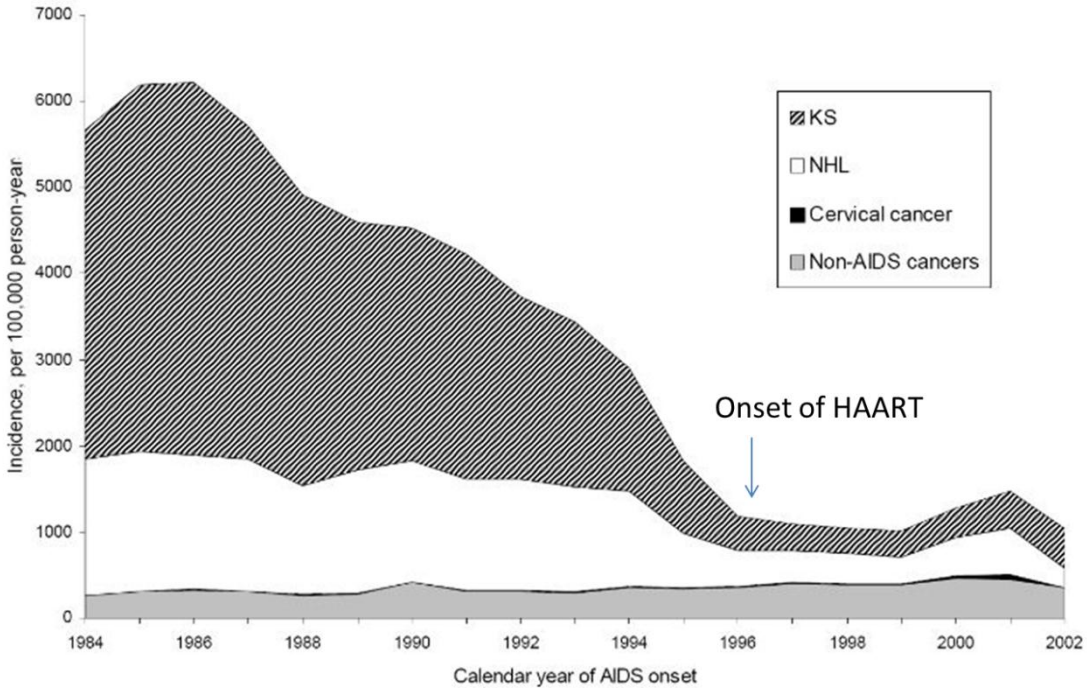
- Lee et al., "*Risk of Cancer among Commercially Insured HIV-Infected Adults on Antiretroviral Therapy*.", J Cancer Epidemiol. **2016**;2016:2138259. Epub 2016 Nov 2, https://www.ncbi.nlm.nih.gov/pubmed/27882054

"*Commercially insured,* ***treated HIV-infected adults had elevated rates for infection-related cancers****, but not for common non-AIDS defining cancers*."

The discussion on cancer and HAART seems bizarre, taking into account that in 1996, when HAART therapy was introduced, the numbers for AIDS-defining cancers had already fallen sharply, cf.

- Engels, "*Non-AIDS-defining malignancies in HIV-infected persons: etiologic puzzles, epidemiologic perils, prevention opportunities*.", AIDS. **2009** May 15;23(8):875-85, https://www.ncbi.nlm.nih.gov/pubmed/19349851

"*HAART substantially reduces risk of KS and EBV-related NHL (11-13).* ***For unknown reasons, KS and NHL incidence rates were falling even during the 1980s and early 1990s among people with AIDS in the U.S.,*** *but introduction of HAART in 1996 led to a further drop (Figure 1).*"



(*Figure 1 from Engels et al. 2009, Cancer incidence among people with AIDS in the U.S. (1984-2002). Incidence is shown as a function of calendar year of AIDS onset for Kaposi sarcoma (KS), non-Hodgkin lymphoma (NHL), cervical cancer, and non-AIDS-defining cancers. Incidence estimates for each cancer are stacked on top of each other, to depict the proportion of total cancer incidence contributed by each cancer type. Data pertain to the two-year period following AIDS onset. Data are from the HIV/AIDS Cancer Match Study.)*

(KS = Kaposi Sarkoma, NHL = Non-Hodgkin-Lymphoma, Cervical Cancer, all 3 are **AIDS-defining** according to the WHO)

Personally, I do not see the drop around 1996 associated with the introduction of HAART, at least not in relation to before 1996. But I see a rise since 1999. In the literature, the decrease, also before 1996, is sold as a success of HAART Therapy.

Maybe it had just been talked about in risk groups that nitrites are a problem? The problems were known, see below. What effect has had the education on AIDS, regardless of HAART?

4.3. HAART and the *Immune Reconstitution Inflammatory Syndrome* (IRIS)

The side effects of HAART can also be sugarcoated by attributing them after years of treatment to an *immune response disease* (IRD), **based solely on CD4 cell count and viral load**, cf.

- Hsu et al., "*Short Communication: Hyperthyroidism in Human Immunodeficiency Virus Patients on Combined Antiretroviral Therapy: Case Series and Literature Review*", AIDS RESEARCH AND HUMAN RETROVIRUSES, Volume 32, Number 6, **2016**, https://www.ncbi.nlm.nih.gov/pubmed/26887978

"*We describe an HIV-infected patient initiated on combined antiretroviral therapy (cART) who subsequently developed* ***immune restoration disease (IRD)*** *hyperthyroidism -* ***this case represents one of five such patients*** *seen at our center within the past year*"

*"****Twenty-three months after initiating cART****, he developed heat intolerance, palpitations, tremors, and reast tenderness. Physical examination demonstrated a diffusely enlarged thyroid without nodularity, bilateral gynecomastia, and a fine resting tremor. His CD4 count was 486 cells/µl (24% CD4cells) and his HIV viral load was undetectable (<40 copies/ml)"*

"Similar to the case patient, at the time of cART initiation, these patients had low baseline CD4 counts (median baseline CD4 of 6.5 [range 3–40] cells/µl) and high viral loads (median 4.19 [range 3.36–5.38] log_{10} copies/ml), and all had been ***on cART for several years*** *(median interval of 38.5 [range 23– 93] months)* ***before the development of hyperthyroidism****"*

- Fournier et al., "*Immune Reconstitution Inflammatory Syndrome Unmasking or Worsening AIDS-Related Progressive Multifocal Leukoencephalopathy: A Literature Review*", Front Immunol. **2017**; 8: 577, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5440580/

"*Although classical PML has declined with cART, PML-IRIS now accounts for up to* ***25% of PML cases diagnosed in HIV-infected patients during the cART era.****"*

- Walker et al. "*The tuberculosis-associated immune reconstitution inflammatory syndrome: recent advances in clinical and pathogenesis research.*", Curr Opin HIV AIDS. **2018** Aug 18 [Epub ahead of print], https://www.ncbi.nlm.nih.gov/pubmed/30124473

"*The incidence of paradoxical TB-IRIS is estimated at 18% (95% CI 16-21%), higher than previously reported and may be over 50% in high-risk groups.* ***Early ART initiation in TB patients increases TB-IRIS risk by greater than two-fold****, but is critical in TB patients with CD4 counts less than 50 cells/µl because it improves survival*"

Tuberculosis is AIDS-defining, which plays a major role for developing countries. As shown below, the CD4 cell count has almost no diagnostic significance, as the values may be transiently and also permanently low in HIV-negative individuals. At the same time, the CD4 cell count in HIV-negative tuberculosis patients is strongly reduced, see below.

Is fire fought with fire here? And if so, can one talk about it? And what if it burns somewhere else? In this situation, a uniform scientific opinion is certainly helpful.

In addition, approximately 75% of the causes of death of HIV+ persons in France do not relate to AIDS-defining diseases anymore but correspond directly to the described side effects of HAART, cf. HIV book, Hoffmann and Rockstroh, https://www.hivbuch.de/wp-content/uploads/2017/04/hiv2016-17_fix.pdf (p. 139):

Tabelle 4.3: Todesursachen bei HIV-Patienten in Frankreich (Morlat 2014)

	2000 (n=964)	2005 (n=1042)	2010 (n=728)
AIDS-definierende Erkrankungen	47 %	36 %	25 %
Nicht-AIDS-definierende Tumoren	11 %	17 %	22 %
Lebererkrankungen	13 %	15 %	11 %
Kardiovaskuläre Erkrankungen	7 %	8 %	10 %
Suizid	4 %	5 %	3 %

(*from Hoffmann und Rockstroh, HIV Buch, 2016/17, p. 139, Causes of death of HIV+ patients in France*)

„Nach dieser Untersuchung stirbt heute nur noch jeder vierte Patient letztlich an AIDS. Andere Erkrankungen wie Tumoren oder (meist Hepatitis-bedingte) Lebererkrankungen nehmen an Bedeutung zu."

Translation:

„According to this study, only one in four patients dies of AIDS today. Other diseases such as tumors or (usually hepatitis-related) liver diseases are becoming more important."

One should perhaps ask: what exactly do we mean by an AIDS dead and what is the purpose of this therapy? Where is the good news? A suicide rate of about 3 - 5% shows under what pressure these people are.

Other studies see the proportion of AIDS-defining diseases as the cause of death of HIV patients even lower, but with the same high portion of cardiac diseases, liver diseases, non-AIDS defining infections and suicides, cf.

- Lifson et al, "*Determination of the underlying cause of death in three multicenter international HIV clinical trials*.", HIV Clin Trials. **2008** May-Jun;9(3):177-85, https://www.ncbi.nlm.nih.gov/pubmed/18547904

"*Of 453 deaths reported through January 14, 2008, underlying causes were as follows:* ***10% AIDS-defining diseases****, 21% non-AIDS malignancies, 9% cardiac diseases, 9% liver disease, 8% non-AIDS-defining infections, 5% suicides, 5% other traumatic events/accidents, 4% drug overdoses/acute intoxications, 11% other causes, and 18% unknown.*"

- Reisler et al., "*Grade 4 events are as important as AIDS events in the era of HAART.*", J Acquir Immune Defic Syndr. **2003** Dec 1;34(4):379-86, https://www.ncbi.nlm.nih.gov/pubmed/14615655

"*Data were analyzed from 2,947 patients enrolled from December 1996 through December 2001.* ***All patients were to receive antiretrovirals*** *throughout follow-up.*"

"During follow-up, 675 patients experienced a grade 4 event (…); 332 developed an AIDS event (…); and ***272 died*** *(…). The most common grade 4 events were liver related (148 patients, …).* ***Cardiovascular events were associated with the greatest risk of death*** *(…)."*

Is this a successful therapy?

- Weldegebreal et al., "*Magnitude of adverse drug reaction and associated factors among HIV-infected adults on antiretroviral therapy in Hiwot Fana specialized university hospital, eastern Ethiopia*.", Pan Afr Med J. **2016** Jul 20;24:25, https://www.ncbi.nlm.nih.gov/pubmed/27800108

"The overall prevalence of Adverse Drug Reaction among Human immunodefiecency virus infected patients in this study was ***17% and more common on those patients taking Stavudine*** *based regimen.* ***Lipodystrophy and peripheral neuropathy were significantly associated with stavudine-based regimens, while anaemia was significantly associated with zidovudine based regimens****."*

- Abdissa et al., "*Adverse drug reactions associated with antiretroviral treatment among adult Ethiopian patients in a tertiary hospital*.", Ethiop Med J. **2012** Apr;50(2):107-13, https://www.ncbi.nlm.nih.gov/pubmed/22924279

*"****ADRs occurred frequently in patients receiving ART****. Grade III/IV toxicity that required withholding or change of treatment occurred in nearly 10% of the patients."*

- Hart et al. "*Inflammation-Related Morbidity and Mortality Among HIV-Positive Adults: How Extensive Is It?*", J Acquir Immune Defic Syndr. **2018** Jan 1;77(1):1-7, https://www.ncbi.nlm.nih.gov/pubmed/28991883

"A shift from AIDS-related causes of morbidity and mortality to non-AIDS causes such as ***non-AIDS malignancy****,* ***liver cirrhosis****,* ***end stage renal disease*** *and* ***serious cardiovascular events*** *occurred in HIV patients nearly one decade ago* ***due to use of potent antiretroviral therapy****."*

"Consistent with two other reports which included participants with lower CD4+ counts, we show that grade 4 events are a major source of morbidity among participants with HIV [26, 27]. Among the participants in our cohort, all of whom had CD4+ counts ≥ 300 cells/mm3 at study entry, the rate of grade 4 events was 3 to 6 times higher than AIDS, CVD (expanded to include less serious events and CVD events that did not meet ERC criteria) or non-AIDS cancer considered separately and was higher than the rate for these three outcomes considered as a single composite outcome."

*"****Everyone in our investigation was taking suppressive ART****. Thus, we can only speculate whether the grade 4 events are due to underlying HIV disease or to ART."*

As of **2018**.

In *Hoffmann* and *Rockstroh* also again, the immune reconstitution syndrome (IRIS), which does not focus on the serious side effects of the drugs, but on the fact that they worked too well. From the HIV book, Hoffmann and Rockstroh, https://www.hivbuch.de/wp-content/uploads/2017/04/hiv2016-17_fix.pdf (p. 138/139):

„Unterschieden werden muss das klinische Versagen, das durch eine versagende ART entsteht, von dem klinischen Versagen, dass darauf zurückzuführen ist, dass schlicht zu spät mit ART begonnen wurde. Das gilt zum Beispiel für Immunrekonstitutionssyndrome, bei denen sich präexistente, subklinische Infektionen in den ersten Wochen nach Beginn einer antiretroviralen Therapie manifestieren (siehe auch Kapitel AIDS). ***Eine OI bei steigenden CD4-Zellen bedeutet daher nicht unbedingt ein Versagen der ART, sondern eher, dass das Immunsystem, vereinfacht gesagt, seine Arbeit wieder aufnimmt.****"*

Translation:

„A distinction must be made between the clinical failure caused by a malfunctioning ART and the clinical failure resulting from the fact that ART was started too late. This applies, for example, to immune reconstitution syndromes in which preexisting, subclinical infections manifest themselves in the first few weeks after initiation of antiretroviral therapy (see also chapter AIDS). ***An OI and increasing CD4 cells therefore does not necessarily mean a failure of the ART, but rather that the immune system, simply put, resumes its work.****"*

Others believe that this effect can be observed after years of HAART, see above. But, what an argument. The therapy starts without any symptoms. But, if HAART goes awry, it was the immune system itself. Basically nobody can lose here, nobody but the patient. But it is a pseudo-argument, because a person who has been HIV+ measured and is not otherwise ill is not immunosuppressed, i.e. his or her immune system works perfectly. Only a fraction of its CD4 cells are infected at all and CD4 cells are produced in large numbers every day. Nothing sets in anew. See below for CD4 cell count, PCR viral load and the bystander cell problem.

But it shows very well what 12 conflicts of interest may cause. The drugs have no side effects anymore. They are too effective (!).

A scenario consistent with all data is that HIV+ people are by no means living longer through HAART.

Because of lower doses today, they die less early.

Cf. also

- Cotton et al., "*A prospective study of the immune reconstitution inflammatory syndrome (IRIS) in HIV-infected children from high prevalence countries*.", PLoS One. **2019** Jul 1;14(7):e0211155, https://www.ncbi.nlm.nih.gov/pubmed/31260455

"The main diagnostic criterion for IRIS was a new or worsening inflammatory event after initiating antiretroviral therapy (ART)."

"Thirty-eight participants (18.8%) developed 45 IRIS episodes. Median time to first IRIS event was 21 days (IQR 13.5 to 55) (range: 4 to 105 days). Sixteen episodes (35.6%) occurred in the first 14 days of ART and 7 (15.6%) after day 60."

*"IRIS was **implicated** in one of three deaths of children with* IRIS *(…). Including the one fatality, 7 participants (18.4%) had severe IRIS (…)."*

"IRIS can also occur in children with asymptomatic HIV disease and high CD4 counts, as noted in our study."

The last statement (from ***2019***) is particularly interesting: with a high CD4 cell count, children are not immunosuppressed even according to this definition.

4.4. Adverse effects of HAART in HIV-negative persons

This view is backed up by cases of **HIV-negative people** who have been **misdiagnosed** and treated wrongly with antiviral drugs. Here are some examples of wrong treatment and several years of HAART. Cf.

Audrey Serrano, Fitchburg, MA, USA: HIV-

- AP, "*Woman Misdiagnosed With HIV Awarded $2.5M*", December 13, **2007**, https://www.cbsnews.com/news/woman-misdiagnosed-with-hiv-awarded-25m/

*"A jury has awarded $2.5 million in damages to a woman who received **HIV treatments for almost nine years** before discovering she never actually had the virus that causes AIDS."*

*"In her lawsuit against a doctor who treated her, Audrey Serrano said the powerful combination of drugs she took triggered a string of ailments**, including depression, chronic fatigue, loss of weight and appetite and inflammation of the intestine.**"*

Weight loss is AIDS-defining.

Many of these media articles focus on social exclusion and stigma. However, this is about the reported adverse effects that cannot be foisted on a putative virus. This should not diminish the social impact of the misdiagnosis and the suffering of these people. On the contrary, it is very likely that social isolation has very negative physical consequences.

Suthida Saengsumat, Bangkok, Thailand: HIV-

- P. Charoensuthipan, Bankok Post, „*Woman's 12-year HIV nightmare finally ends*", **1 Jun 2017**, https://www.bangkokpost.com/news/general/1260602/womans-12-year-hiv-nightmare-finally-ends

"Suthida Saengsumat, 20, went to the centre in Bangkok for a second HIV test on Thursday, after a previous test there on May 23 showed she was HIV-negative."

"Dr Sombat Thanprasertsuk, of the Disease Control Department, said doctors were now concerned about the ***side effects of the HIV medication Ms Suthida had been taking since a child and until comparatively recently****."*

On the same case, cf.

- P. Charoensuthipan, Bankok Post, "*Tests confirm 'HIV woman' is virus-free*", 2 Jun **2017**, https://www.bangkokpost.com/news/general/1260735/tests-confirm-hiv-woman-is-virus-free

"Asked what else could cause that extremely low CD4 count if it was not HIV, Dr Prapan said flu infections or other types of virus can cause a decreased CD4 count, ***but these types of virus should never cause a CD4 count that was as low as Ms Suthida's had been.****"*

And

- Tanveer Mann, Metro, "*Woman sues after she was wrongly diagnosed with HIV as a child*", 3 Jun **2017**, https://metro.co.uk/2017/06/03/woman-sues-after-she-was-wrongly-diagnosed-with-hiv-as-a-child-6681812/

"Suthida had to take anti-retroviral drugs every day since her diagnosis at eight-years-old, but stopped five years ago when she was first pregnant."

43 years old married woman, Malawi, reported by Nyirenda Mulinda: HIV-

- Mulinda et al., "*HIV test misdiagnosis*", Malawi Med J. **2011** Dec; 23(4): 122–123, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3588573/

"*A 43 years old married woman presented to a private clinic with repeated episodes of mouth sores. The clinician diagnosed her with oral candida*."

(A candida infection of the throat is AIDS defining)

"The HIV rapid test came out positive. Her family including the husband and two children tested HIV negative. ***After some discussion, the clinician recommended that she should start ART. She was started on a combination of d4T, 3TC and nevirapine.***"

*"****A diagnosis of lipodystrophy was made, and the patient's treatment was changed to AZT/3TC/NVP****. She took this regimen for 2 years (2007).* ***In 2008, she developed anaemia thought to be secondary to AZT. As a result her treatment was changed to TDF/3TC/EFV****. . She took this regimen faithfully till May 2011."*

"*She was informed of the results and advised to stop HIV treatment and return in 3 months for repeat tests. The repeat tests were unchanged.* ***It was concluded that this lady was never HIV positive****."*

"*For this woman, the reason for her oral thrush was very clear.* ***Prolonged use of steroids is a well known cause.***"

Yang Shoufa, Henan, China: HIV-

- Asia One, "*Man misdiagnosed with HIV 'lived in hell' for 10 years*", May 20, **2016**, http://www.asiaone.com/health/man-misdiagnosed-hiv-lived-hell-10-years

*"For the next eight years, Mr Yang **spent his life savings on anti-HIV drugs**. However, his condition deteriorated."*

"While warded there, his medical reported revealed that he did not have AIDS. Multiple tests done at other hospitals also confirmed that he was HIV-negative, CCTV News reported."

*"He was diagnosed with a slew of other illnesses instead, which included **inflammation of the esophagus and gallbladder, bleeding from stomach ulcers and an enlarged prostate**."*

In contrast, the statement of an executive director of the Center for HIV Law and Policy in New York sounds cynical that doctors do not have the last word, but that this is with the patient.

Terry Hedgepeth, Washington D.C., USA: HIV-, not treated

- Keith Alexander, Washington Post, "*Man misdiagnosed with HIV settles suit against Whitman- Walker Clinic*", August 10, **2012**, https://www.washingtonpost.com/local/crime/man-misdiagnosed-with-hiv-settles-suit-against-whitman--walker-clinic/2012/08/10/67be2a02-e328-11e1-a25e-15067bb31849_story.html

"*Catherine Hanssens, executive director of the Center for HIV Law and Policy in New York, said that courts and juries realize doctors make mistakes."*

"'*Most people who find out they are **not HIV-positive** view it as good news — they don't run out and get a lawyer,' Hanssens said."*

"'***Doctors are not infallible, and patients have to realize [the doctors] don't, and should not, have the last say in their health***.'"

How far does this statement apply? Does it also apply to biomedical research? I think we're doing exactly the right thing here; we're looking for what's in the original literature.

Farida Kiconco, Sheema, Uganda: HIV-

- Adolf Ayoreka, "*Woman tested negative after six years on ARVs*", 9th August **2018** https://www.newvision.co.ug/new_vision/news/1483178/woman-tested-negative-arvs-settlement

"Kiconco, a resident of Rwengando parish Kiziba, Kagango division in Sheema Municipality on March 16, 2011 sought medical attention on account of her pregnancy and went to Kabwohe Health centre IV, the attending physician requested for an HIV test. Samples were taken and came back positive."

"She was prescribed with septrin, which she took until she was introduced to ARVS after giving birth."

"Faridah Kiconco sued Sheema Municipal council and Sheema local government after their medical personnel at Kabwohe health centre IV reportedly delivered wrong test results and started her on ARVs for six years ***when she was HIV negative****."*

"As a result, Farida developed ***adverse health conditions*** *for which she sought treatment at Mbarara Muslim health centre but* ***have continued to persevere****."*

"I still have much ***abnominal pain, I was told that my liver and lungs were affected*** *so I need a lot of money for treatment if possible I can be taken to India."*

On the same case:

- Victoria Namutebi Wamala, *„Ugandan woman wrongly diagnosed with HIV in 2011 suffers ARV effects*", Africanews 26/12/**2017**, http://www.africanews.com/2017/12/26/ugandan-woman-wrongly-diagnosed-for-hiv-in-2011-suffers-arv-effects/

"*The 28 year old mother of three is suffering a* ***severe sickness after taking Anti-Retroviral Drugs****, ARVs for the past six years yet* ***she is HIV negative***."

"Farida said: 'Dr. Tusiime did a blood test after which he advised me to stop taking ARVs because I was HIV negative. He referred me to Mbarara referral hospital for further treatment. Mbarara hospital too confirmed that ***I was HIV negative****.'"*

"You know these ARVs you take them for long…It is taken daily for many many years. So it means that if it was like a mistake for a day or two, that one at least it can understood. But if you continuously take those drugs when you are not infected, then the liver will be damaged including other organs in your body. It is not good," he stressed."

Elizabeth Zighe Mwakazi, Kwale, Kenya: HIV-

- Eunice Kilonzo, "*Woman who was given wrong HIV diagnosis to get final results soon*", November, 21 **2016**, https://www.nation.co.ke/news/Woman-misdiagnosed-with-HIV-to-get-final-results-soon/1056-3459000-b6ov2i/index.html

"Ms Mwakazi was misdiagnosed with HIV in July at Diani Health Centre, where she had gone for an ante-natal check-up. ***On the fourth day of taking ARVs, she experienced side-effects such as dizziness, nausea and vomiting, shivers and serious body weakness. Her son suffered similar symptoms and also severe skin rashes, irritability and loss of weight and appetite.****"*

Weight loss is AIDS defining.

Peter Mungai Njoroge, Nairobi, Kenya: HIV-

- Carole Maina, "*Man wrongly diagnosed with HIV and TB sues KNH*", Jun. 06, **2014**, https://www.the-star.co.ke/news/2014/06/06/man-wrongly-diagnosed-with-hiv-and-tb-sues-knh_c950659

"*Peter Mungai Njoroge received Tubercolusis and HIV treatment for several months before he was told that he never actually had the virus that causes AIDS."*

"*Now, the middle aged man lost his wife following the mis-diagnosis that **left him paralyzed on one side of his body.***"

"*Mungai says that as a result of the negligent and wrong diagnosis of Hospital, the anti-retroviral drugs that he diligently took to fight the killer disease has caused him a lot of **pain**, **psychological torture, loss of erection**, **loss of his marriage** and **left him paralyzed**. He says the he returned to KNH to do another test and the doctors confirmed that **he was indeed HIV negative**."*

On the same case, cf.

- Carole Maina, "*Kenya: Man Wrongly Diagnosed With HIV and TB Sues KNH*", 6 June **2014**, https://allafrica.com/stories/201406090053.html

"Now, the middle aged man lost his wife following the mis-diagnosis that left him paralyzed on one side of his body."

However, the harmful adverse effects that affect the liver, among other things, are not limited to HIV-infected people. These harm HIV + people in the same way. If you cannot distinguish for many years the symptoms of the disease from the adverse effects of the medication, then you have a problem.

James Malone, Hayward, CA, USA: HIV-

- Julian Guthrie, SF Chronicle, "*HAYWARD / False diagnosis of HIV discovered after 8 years / Veteran's life severely affected after VA doctor made mistake*" ,August 28, **2004**, https://www.sfgate.com/health/article/HAYWARD-False-diagnosis-of-HIV-discovered-after-2729917.php

"Earlier this month, Malone, 59, was summoned to his doctor's office. He listened as the doctor delivered the stunning news: He is HIV negative."

"'An HIV-positive person can have good T-cell counts and undetectable viral loads over a long period of time," Pridmore said. "And in this case, the patient exhibited symptoms that could be consistent with an HIV diagnosis.'"

Before that sounded a bit different.

*„In a September 2003 letter from Karp, Malone was classified as "permanently disabled and unable to work or participate in any stressful situation whatsoever." His medical prognosis was deemed "very poor." The letter said Malone **was being treated for 20 medical conditions**, the first condition being HIV. The sixth item on the list, nausea and vomiting, was said to be "**related to condition 1**."*

*„Malone, who is thin and voluble and walks with a cane, said that **he attributed his frequent nausea, vomiting, diarrhea and weight loss to being HIV-positive.**"*

(James Malone, after 8 years of HAART though HIV-, shows a selection of his medicines to treat the 20 different medical conditions that HAART has caused him.)

Weight loss is AIDS defining. Mr. Malone died shortly after the article was published.

Bobby Russell, Lexington, KY, USA: HIV-

- Anna Rodgers, "*Man Spent 8 Years Taking Highly Toxic Drugs Only To Find Out He Was Misdiagnosed With HIV*", April 3, **2015,** https://www.collective-evolution.com/2015/04/03/man-spent-8-years-taking-highly-toxic-drugs-only-to-find-out-he-was-misdiagnosed-with-hiv/

"***Tragically, Bobby today is now at risk of developing other health problems associated with the toxic effects from the HAART medications. These drugs aren't your average over-the-counter drugs*** *– they are available only by prescription and have clearly listed adverse reactions and side effects."*

"*Today, Bobby is still not well enough to work, and can barely afford to support himself. He needs money to sue and money to get his health back on track****. He needs to start taking supplements which can help repair some of the damage done by these drugs****. This is not a case of someone taking some standard over the counter drugs for nearly 9 years –* ***this is almost a decade of taking some of the*** *most* ***extreme medications on the planet.****"*

"***Supplements to repair the damage***". Like Scott Jordan, HIV+, see above.

On the same case, cf.

- Hunter Stuart, "*Bobby Russell, U.S. Veteran, Files Lawsuit Claiming HIV Misdiagnosis*", 09/03/**2013**, https://www.huffingtonpost.com/2013/09/03/bobby-russell-hiv-veteran-sues-hospital_n_3860308.html?guccounter=1

*"Daily told HuffPost that **Russell was taking up to 15 pills a day to treat his supposed HIV**, and his drug regimen **included azidothymidine** (commonly known as **AZT**), a drug whose safety has been questioned after experiments **showed it to be carcinogenic in rodents**. "All this medication has taken a toll on [Russell's] body," Daily explained."*

How can it be that these men and women are treated with antiviral drugs for years(!) and it is not at all noticed that these "*patients*" are HIV-negative?

Because they show no symptoms other than the side effects of the drugs.

And what about the famous therapy control by CD4 cell count and PCR viral load?

What is common to all cases above, besides the stigma and severe adverse effects of HAART, is the passivity of the doctors who set up the original diagnosis. HIV = AIDS is the dogma and none of the attending physicians seems to have ever dealt with the contradictions and unanswered questions of the HI virus hypothesis and the HAART therapy. With very few exceptions, I have not met a doctor on this topic, who does not talk down the serious adverse effects or refers to it as "***initial problems from the 90s***". The "***beneficial***" HAART is the consensus therapy, the end.

In any case, the side effects in HIV-negative and misdiagnosed individuals strongly speak against the very useful and convenient *Immune Reconstitution Inflammatory Syndrome* (IRIS).

I am not aware of any scientific investigation that systematically reviews these cases of misdiagnosis and serious side effects of HAART, and in particular the distinction of these side effects from AIDS symptoms.

Summary: adverse effects of HAART in **HIV-negative** (misdiagnosed) people

James Malone, Hayward, CA, USA	treated for 20 medical conditions, the first condition being HIV; frequent nausea, vomiting, diarrhea and weight loss
Bobby Russell, Lexington, KY, USA	not well enough to work, taking supplements to repair some of the damage, taking up to 15 pills a day
Audrey Serrano, Fitchburg, MA, USA	depression, chronic fatigue, loss of weight and appetite and inflammation of the intestine
Peter Mungai Njoroge, Nairobi, Kenya	pain, loss of erection, paralyzed on one side of his body

Elizabeth Zighe Mwakazi, Kwale, Kenya	dizziness, nausea and vomiting, shivers and serious body weakness
Farida Kiconco, Sheema, Uganda	abnominal pain, liver and lungs affected, severe sickness after taking Anti-Retroviral Drugs
43 years old married woman, Malawi, reported by Nyirenda Mulinda	Lipodystrophy, anaemia
Suthida Saengsumat, Bangkok, Thailand	stopped HAART 5 years ago, doctors concerned about the side effects of the HIV medication
Yang Shoufa, Henan, China	inflammation of the esophagus and gallbladder, bleeding from stomach ulcers and an enlarged prostate

(Table: side effects of HAART in HIV-negative people)

Here are a few studies on the effect of so-called protease inhibitors on ***HIV-negative people***. These are part of the combined preparations, which are given as HAART to HIV+ measured people, cf.

- Noor et al, "*Metabolic effects of indinavir in **healthy HIV-seronegative men***.", AIDS. **2001** May 4;15(7):F11-8, https://www.ncbi.nlm.nih.gov/pubmed/11399973

***"In the absence of HIV infection, treatment with indinavir for 4 weeks causes insulin resistance** independent of increases in visceral adipose tissue or lipid and lipoprotein levels*."

- Lee et al., "*The acute effects of HIV protease inhibitors on insulin suppression of glucose production in **healthy HIV-negative men***.", J Acquir Immune Defic Syndr. **2009** Oct 1;52(2):246-8, https://www.ncbi.nlm.nih.gov/pubmed/19680131

***"Some PIs can acutely blunt the ability of insulin to suppress EGP**, but, as with insulin resistance, the effects of PIs on EGP are drug-specific, not class-specific."*

- Lee et al., "*Effects of ritonavir and amprenavir on insulin sensitivity **in healthy volunteers***.", AIDS. **2007** Oct 18;21(16):2183-90, https://www.ncbi.nlm.nih.gov/pubmed/18090045

*"Compared to previously performed studies of identical design using single doses of indinavir and lopinavir/ritonavir, **a hierarchy of insulin resistance was observed** with the greatest effect seen with indinavir followed by ritonavir and lopinavir/ritonavir, with little effect of amprenavir*."

4.5. Adverse effects of PrEP/PEP in HIV-negative persons

The observations above are confirmed by the side effects of the so-called pre-exposure prophylaxis (PrEP) for ***HIV-negative*** people to prevent a supposed infection and which consists of drugs that are also used in HAART, with similar side effects, cf.

- Tetteh et al., "*Pre-Exposure Prophylaxis for HIV Prevention: Safety Concerns*.", Drug Saf. **2017** Apr; 40(4):273-283, https://www.ncbi.nlm.nih.gov/pubmed/28130774

"*Side effects considered potentially serious in the daily use of Truvada or TDF for PrEP are* ***liver function problems, kidney damage, hypophosphatamia, proteinaemia*** *or* ***glucosuria, pancreatitis, bone thinning*** *and* ***lactic acidosis****.* ***Flu-like symptoms, hypertriglyceridemia, increased creatinine phosphokinase, unusual dreams*** *and* ***hyperpigmentation*** *are associated with the use of FTC*."

"*Major concerns are renal, hepatic and bone toxicity, but these are transient and non-progressive* ***and quickly resolved after discontinuation of TDF***."

- Patel et al., "*Serious adverse cutaneous and hepatic toxicities associated with nevirapine use by* ***non-HIV-infected individuals***.", J Acquir Immune Defic Syndr. **2004** Feb 1;35(2):120-5, https://www.ncbi.nlm.nih.gov/pubmed/14722442

"Twelve ***non-HIV-infected individuals*** *developed severe cutaneous toxicity, including 3 with Stevens-Johnson syndrome, after 7 to 12 days of nevirapine-containing PEP regimens.* ***Thirty non-HIV-infected individuals*** *developed hepatotoxicity after 8 to 35 days of single-agent nevirapine (n = 8) or a nevirapine-containing PEP regimen (n = 22). Findings included ECOG grade 3 or 4 hepatotoxicity (n = 14), fevers (n = 11), skin rashes (n = 8), eosinophilia (n = 6), and fulminant hepatic necrosis requiring an orthotopic liver transplant (n = 1)."*

"Serious hepatic and cutaneous toxicities can occur in ***non-HIV-infected individuals*** *who receive short-term nevirapine therapy. The rate of severe hepatotoxicity appears to be greater in non-HIV-infected individuals than in HIV-infected persons and may be associated with higher CD4 counts.* ***The use of PEP regimens containing nevirapine should be discouraged.****"*

- Liu et al., "*Bone Mineral Density in* ***HIV-Negative Men*** *Participating in a Tenofovir Pre-Exposure Prophylaxis Randomized Clinical Trial in San Francisco*", PLoS One. **2011**; 6(8): e23688, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3163584/

"Ten percent of HIV-negative MSM had low BMD at baseline. ***TDF use resulted in a small but statistically significant decline in BMD at the total hip and femoral neck****. Larger studies with longer follow-up are needed to determine the trajectory of BMD changes and any association with clinical fractures."*

- Kasonde et al., "*Bone mineral density changes among **HIV-uninfected young adults** in a randomised trial of pre-exposure prophylaxis with tenofovir-emtricitabine or placebo in Botswana*.", PLoS One. **2014** Mar 13;9(3):e90111, https://www.ncbi.nlm.nih.gov/pubmed/24625530

*"Use of TDF-FTC was associated with a **small but statistically significant decrease in BMD** at the forearm, hip and lumbar spine. A high percentage (6.8%) of healthy Batswana young adults had **abnormal baseline BMD** Further evaluation is needed of the longer-term use of TDF in HIV-uninfected persons."*

- Owino et al., "*Neurological syndrome in an **HIV-prevention trial** participant randomized to daily tenofovir disoproxil fumarate (300 mg) and emtricitabine (200 mg) in Bondo, Kenya*", Int Med Case Rep J. **2013**; 6: 91–93, https://www.ncbi.nlm.nih.gov/pubmed/24353443

"After an additional 4 days, she developed a disabling weakness of her upper limbs and tremors in her hands. The study product was discontinued, and within 2 weeks she was free of all symptoms. One month after restarting the drug, she complained of posture-dependent numbness of her upper limbs."

- Mulligan et al. "*Effects of Emtricitabine/Tenofovir on Bone Mineral Density in **HIV-Negative Persons** in a Randomized, Double-Blind, Placebo-Controlled Trial*", Clin Infect Dis. **2015** Aug 15;61(4):572-80, https://www.ncbi.nlm.nih.gov/pubmed/25908682

*"In **HIV-uninfected persons**, FTC/TDF PrEP was associated with small but statistically significant decreases in BMD by week 24 that inversely correlated with TFV-DP, with more stable BMD thereafter*."

- Chan et al., "*Potential kidney toxicity from the antiviral drug tenofovir: new indications, new formulations, and a new prodrug*", Curr Opin Nephrol Hypertens. **2018** Mar;27(2):102-112, https://www.ncbi.nlm.nih.gov/pubmed/29278542

*"Nephrologists should be aware of the **potential kidney and bone toxicity of TDF**, as well as unique situations in which the newer prodrug TAF may contribute to kidney injury."*

- Glidden et al., "*Brief Report: Recovery of Bone Mineral Density After Discontinuation of Tenofovir-Based **HIV Pre-exposure Prophylaxis***.", J Acquir Immune Defic Syndr. **2017** Oct 1;76(2):177-182, https://www.ncbi.nlm.nih.gov/pubmed/28639995

*"On average, BMD returned to baseline levels **by 1 year after PrEP stop**. Recovery was consistent across age, baseline BMD z-score, and treatment duration."*

- Mirembe et al., "*Bone Mineral Density Changes Among Young, **Healthy African Women** Receiving Oral Tenofovir for HIV Preexposure Prophylaxis*.", J Acquir Immune Defic Syndr. 2016 Mar 1;71(3):287-9, https://www.ncbi.nlm.nih.gov/pubmed/26866954

*"TDF-containing oral PrEP resulted in **small but significant reversible decreases in hip and spine BMD** among young African women."*

Reversible is good, except you are supposed to take the drug for a lifetime.

- Lu et al., "*Tenofovir disoproxil fumarate induces pheochromocytoma cells apoptosis*.", Eur J Pharmacol. **2019** Feb 5;844:139-144, https://www.ncbi.nlm.nih.gov/pubmed/30529468

"Despite the triumph of highly active antiretroviral therapy (HAART) in anti-HIV infection, more than half of the HIV infection individuals receiving antiretroviral therapy acquire HIV-associated neurocognitive disorder (HAND). Previously researches had reported that the ***HAART neurotoxicity is implicated in HAND-related morbidity****."*

*"****TDF has neural toxicity effect that is relevant to the cell apoptosis****, which may be related to the increasing prevalence of HAND."*

- Bertrand et al., "*Cerebral Vascular Toxicity of Antiretroviral Therapy*.", J Neuroimmune Pharmacol. **2019** Jun 17. doi: 10.1007/s11481-019-09858-x, https://www.ncbi.nlm.nih.gov/pubmed/31209776

"Indeed, ***increasing evidence demonstrates that the antiretroviral drugs used for HIV treatment have toxic effects resulting in various cellular and tissue pathologies****."*

*"****A combination of Tenofovir and Emtricitabine can act as cellular stressors****, leading to endothelial cell senescence, as demonstrated by a reduction in proliferation, and an increase in inflammatory markers (Cohen et al. 2018). This results in decreased BBB integrity and impaired endothelial cell functions.* ***Exposure to Efavirenz has been shown to reduce endothelial viability at relatively low concentrations****. This effect has been linked to multiple insults, such as a dysregulation of polymerase γ function, imbalance of intracellular calcium levels and depletion of ADP (Bertrand and Toborek 2015; Weiss et al. 2016; Faltz et al. 2017)."*

- Kichloo et al., "*Tenofovir and Severe Symptomatic Hypophosphatemia*.", J Investig Med High Impact Case Rep. **2019** Jan-Dec;7:2324709619848796, https://www.ncbi.nlm.nih.gov/pubmed/31142127

"Although the initial results of the clinical trials supported the renal safety of Tenofovir, ***clinical use of it has caused a low, albeit a significant, risk of renal damage either in the form of AKI or CKD****. The pathophysiology has been linked to the effect of this medication on the proximal tubular cell. Although the exact mechanism is unknown, studies have suggested that Tenofovir accumulates in proximal tubular cells which are rich in mitochondria."*

"Here we present a case where ***Tenofovir treatment resulted in severe hypophosphatemia*** *requiring hospitalization for parentral phosphate repletion."*

- Suzuki et al., "*Effect of Tenofovir Disoproxil Fumarate on Incidence of Chronic Kidney Disease and Rate of Estimated Glomerular Filtration Rate Decrement in HIV-1-Infected Treatment-Naïve Asian Patients: Results from 12-Year Observational Cohort*.", AIDS Patient Care STDS. **2017** Mar;31(3):105-112, https://www.ncbi.nlm.nih.gov/pubmed/28282247

*"**TDF use was associated with CKD** [odds ratio (OR), 1.8 …]. The cumulative mean loss in the TDF group, relative to the control, increased over time after 1, 4, and 8 years of TDF exposure (-3.8, -5.5, and -9.0 mL/min/1.73 m2, respectively; p < 0.0001).*

The eGFR rapidly declined during the first 3 months of cART, particularly in the TDF group (-26.4 vs. -7.4 mL/min/1.73 m2/year in the control).

***In the TDF group, cART introduction was significantly associated with a faster rate of eGFR decline** (from -0.44 to -2.11 mL/min/1.73 m2/year; p = 0.010), whereas in the control, the difference was not significant.*

***For HIV-1-infected Asian patients with low body weight, TDF-containing cART is associated with CKD and faster eGFR decline**."*

- Keller et al., „*Tenofovir disoproxil fumarate intravaginal ring for HIV pre-exposure prophylaxis in sexually active women: a phase 1, single-blind, randomised, controlled trial*", The Lancer, July 15, **2019**, https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(19)30145-6/fulltext

*"Sexually active women who were **HIV negative** were randomly assigned (3:1) to a tenofovir disoproxil fumarate ring or placebo ring."*

*"…; eight were asked to discontinue ring use early because of **ulcerations (grade 1) near the ring**; in the remaining two women, rings were electively removed by study staff on day 20 and day 23."*

*"…, **all ulcers resolved after ring removal.** No participants in the placebo group developed ulcers."*

*"Concentrations of multiple inflammatory cytokines and chemokines **were significantly higher at days 14 and 28** compared with baseline in the tenofovir disoproxil fumarate ring group but not the placebo group."*

Die Wunderdroge TDF (auch in TRUVADA) versagt im Menschenversuch. Aber

„Future studies are needed …"

- Ascher et al., "*HIV pre-exposure prophylaxis with tenofovir disoproxil fumarate/emtricitabine and changes in kidney function and tubular health*.", AIDS. **2019** Dec 2, [Epub ahead of print], https://www.ncbi.nlm.nih.gov/pubmed/31794523

"Six months of PrEP with TDF/FTC was associated with decreases in eGFRcr and eGFRcys. We also observed for the first time changes in 4 of 14 urine biomarkers reflecting kidney tubular health. These findings demonstrate that PrEP has direct effects on eGFR and the proximal tubule."

- Yazie et al., "*Reduced Kidney Function in Tenofovir Disoproxil Fumarate Based Regimen and Associated Factors: A Hospital Based Prospective Observational Study in Ethiopian Patients*.", Int J Nephrol. **2019** Feb 3;2019:9172607, https://www.ncbi.nlm.nih.gov/pubmed/30863641

"Conclusion: ***The renal dysfunction (defined as decline in eGFR greater than 25%) was found in a quarter of the study population****. The long term impact and the clinical implication of it* ***are not clear****."*

- Michael Carter, "*Cases of hair loss among African-American women reported after switch to new tenofovir formula*", 26 June **2019**, http://www.aidsmap.com/page/3536944/

Dazu

- El Zein et al., „*Alopecia after switch to tenofovir alafenamide in six African American women*.", Open Forum Infectious Diseases, 06 June **2019**, https://academic.oup.com/ofid/advance-article/doi/10.1093/ofid/ofz278/5512421

Note: PrEP is for HIV- people, i.e. **no** HIV.

That means, the side effects are caused solely by the medication.

Are these people really sick? How can it be that people are treated, although essential issues, e.g. what is the disease-causing mechanism, are obviously not known?

It is interesting to note that in a recent trail (*DISCOVER*) by Gilead Science, the manufacturer of TRUVADA to different formualtions of tenofovir were compared. One group took tablets with ***300 mg*** *tenofovir disoproxil fumarate* (TDF) and the other group tablets with ***25*** mg *tenofovir alafenamide* (TAF). This amounts to a dosage reduction of tenofovir of a factor of ***9*** by molecular weight. Cf. on the trial https://clinicaltrials.gov/ct2/show/NCT02842086?term=f%2Ftaf

A considerable improvement of the *kidney values* and the *bone mineral density* was observed, cf.

- "*Results from DISCOVER Trial Provide Bone and Renal Safety Profile Data from Participants who Switched from Truvada for PrEP® to Descovy for PrEP*.", Conference Reports for NATAP, IDWeek October 3 -7, **2018** San Francisco, CA, http://www.natap.org/2019/IDWeek/IDWeek_61.htm

"Improvements were statistically significant as early as Week 4 of the trial. At Week 48, eGFRCG increased by 3.9 mL/min from baseline for those randomized to F/TAF and decreased by 0.6 mL/min in those who continued to receive F/TDF (p<0.001)."

"Participants who were randomized to switch to F/TAF experienced statistically significant improvements in BMD of the hip and spine compared with those randomized to continue F/TDF. In addition, participants taking F/TAF for PrEP were significantly less likely to develop osteopenia of the spine."

The reduction in dosage from ***300 mg*** to ***10 mg*** translates directly to a ***90% lower plasma concentration*** of tenofovir, cf.

- Podany et al., "*Plasma and intracellular pharmacokinetics of tenofovir in patients switched from tenofovir disoproxil fumarate to tenofovir alafenamide*.", AIDS. **2018** Mar 27;32(6):761-765, https://www.ncbi.nlm.nih.gov/pubmed/29334548

*“A single-arm, prospective, nonrandomized, cross-over, pharmacokinetic study in patients receiving a TDF-containing regimen (**TDF 300 mg**/FTC 200 mg/EVG 150 mg/COBI 150 mg) switched to a TAF-containing FDC regimen (**TAF 10 mg**/FTC 200 mg/EVG 150 mg/COBI 150 mg).”*

*“In 30 participants with evaluable data, TFV plasma concentrations **decreased 90%** [TDF: 99.98 (2.24) ng/ml vs. TAF: 10.2 (1.6) ng/ml, P < 0.001] after the switch while cell-associated TFV-DP increased 2.41-fold [TAF: 834.7 (2.49) vs. TDF: 346.85 (3.75) fmol/10 cells, P = 0.004].”*

You might call that a proof.

These data strongly suggest that the issue of HIV / AIDS should be looked at more closely and people and patients should not rely on the "*good cooperation*" of research, industry and the Ministry of Health. These side effects of the cell poisons used would also be extremely demanding on the quality of the diagnosis.

As will be shown below these demands are definitely not met.

4.6. The *TRUVADA* lie

It seems to be the most recent state of research that presumed antiviral drugs prevent HIV transmission in serodiscordant homosexual couples even in unprotected intercourse, cf.

- Rodger et al, "*Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study*", The Lancet, 02.05.**2019**, https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)30418-0/fulltext

Please note 2 things.

As we will see, the lack of transferability of the putative HIV virus is not new, see below for the transmission rate of serodiscordant, heterosexual couples, regardless of sexual practice ***and also without medication!*** On the other hand, this study completely ignores the serious side effects of these substances.

Truvada is one such presumptive anti-viral drug for prophylaxis and has been approved in the US in **2012** and in the EU since August **2016** under the condition of pharmacovigilance. There are currently ***more than 5,400 suspected cases of mostly serious side effects***. See also the European database for suspected cases of drug side effects,

- EudraVigilance, European Database of suspected adverse drug reaction reports, **Truvada**, *Number of Individual Cases by Reaction Groups by Seriousness*, access 04.12.**2019**, http://www.adrreports.eu/en/search.html#

	Number of individual cases			
Reaction Groups\Seriousness	**Non Serious**	**Not Specified**	**Serious**	**Total**
Blood and lymphatic system disorders	12	7	281	**300**
Cardiac disorders	5	0	166	**171**
Congenital, familial and genetic disorders	0	3	216	**219**
Ear and labyrinth disorders	8	2	35	**45**
Endocrine disorders	2	1	47	**50**
Eye disorders	7	3	72	**82**
Gastrointestinal disorders	87	13	628	**728**
General disorders and administration site conditions	75	18	1,782	**1,875**
Hepatobiliary disorders	11	6	441	**458**
Immune system disorders	5	8	230	**243**
Infections and infestations	9	7	556	**572**
Injury, poisoning and procedural complications	53	11	931	**995**
Investigations	129	37	1,341	**1,507**
Metabolism and nutrition disorders	24	13	359	**396**
Musculoskeletal and connective tissue disorders	107	18	997	**1,122**
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	1	2	135	**138**
Nervous system disorders	59	8	462	**529**
Pregnancy, puerperium and perinatal conditions	9	4	301	**314**
Product issues	4	0	12	**16**
Psychiatric disorders	58	6	1,120	**1,184**
Renal and urinary disorders	115	75	1,769	**1,959**
Reproductive system and breast disorders	9	1	53	**63**
Respiratory, thoracic and mediastinal disorders	3	2	185	**190**
Skin and subcutaneous tissue disorders	102	8	456	**566**
Social circumstances	2	0	869	**871**
Surgical and medical procedures	2	0	202	**204**
Vascular disorders	6	6	93	**105**
Total	**634**	**161**	**5,469**	**6,264**

Cf. ibid http://www.adrreports.eu/en/data_source.html

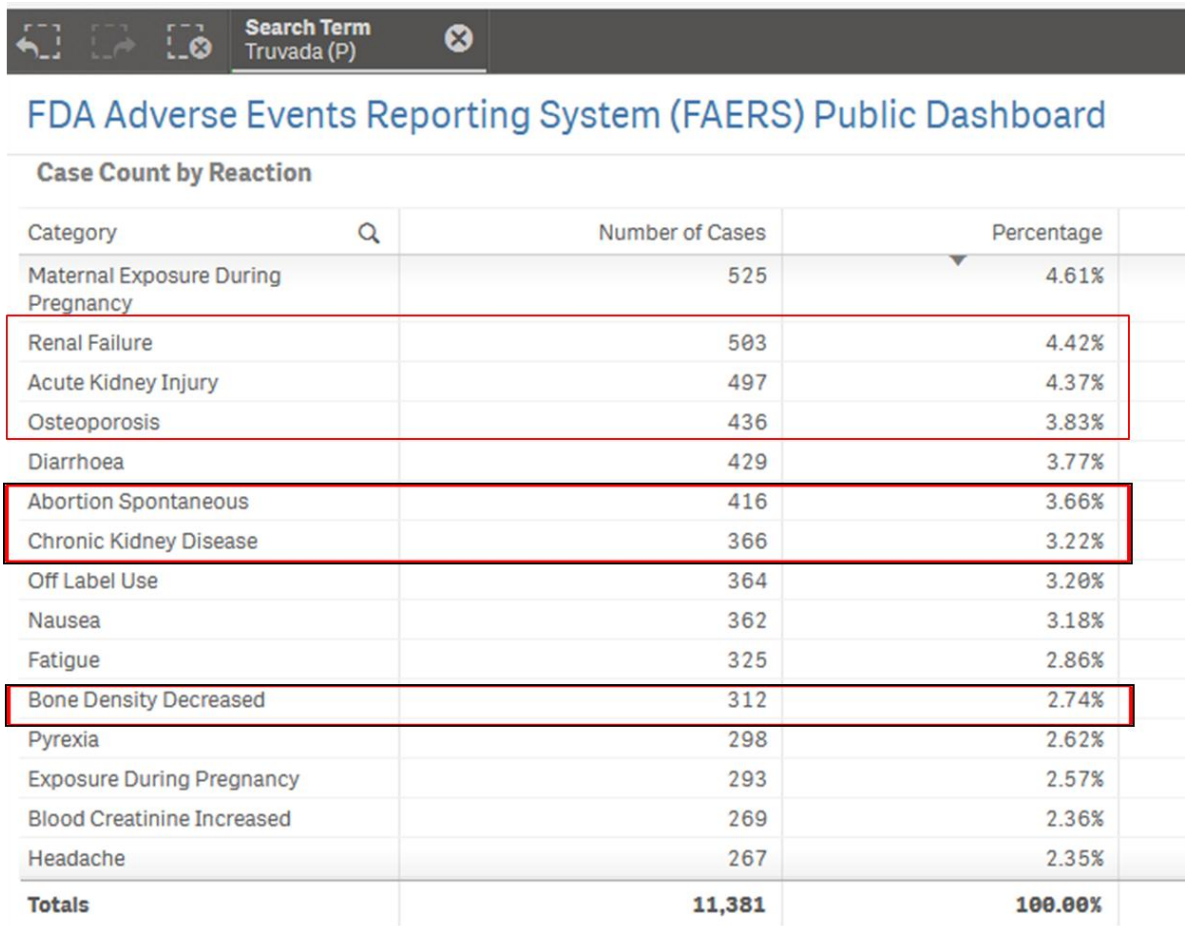
"***A side effect is classified as 'serious'*** *if it (i) results in death, (ii) is life-threatening, (iii) requires hospitalisation or prolongation of existing hospitalisation, (iv) results in persistent or significant disability/incapacity (as per reporter's opinion), (v) is a congenital anomaly/birth defect, or (vi) results in some other medically important conditions."*

"*Reports where medicines or active substances are reported as a* ***concomitant medicine are excluded****."*

The data in the EU database correspond to the data and side effects in the US database of the FDA, cf.

- FDA Adverse Event Reporting System (FAERS) Public Dashboard, https://www.fda.gov/drugs/fda-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard or https://fis.fda.gov/

TRUVADA, access 04.12.**2019**,



Category	Number of Cases	Percentage
Maternal Exposure During Pregnancy	525	4.61%
Renal Failure	503	4.42%
Acute Kidney Injury	497	4.37%
Osteoporosis	436	3.83%
Diarrhoea	429	3.77%
Abortion Spontaneous	416	3.66%
Chronic Kidney Disease	366	3.22%
Off Label Use	364	3.20%
Nausea	362	3.18%
Fatigue	325	2.86%
Bone Density Decreased	312	2.74%
Pyrexia	298	2.62%
Exposure During Pregnancy	293	2.57%
Blood Creatinine Increased	269	2.36%
Headache	267	2.35%
Totals	**11,381**	**100.00%**

Truvada is mainly used for prophylaxis (PrEP) but also for therapy. However, putting this variety of different side effects on one suspected virus is too easy (see also below on the so-called *HIV-related diseases*). When it comes to prophylaxis, we speak of ***HIV-negative people***.

It makes sense to look at the list of conflicts of interest of the scientists involved in *Rodger et al*., cf. ibid,

"Declaration of interests

*VE reports grants from **MSD**, personal fees and non-financial support from **Gilead**, and personal fees from **Janssen** and **Bristol-Myers Squibb**.*

*AMG has received funding from **Cepheid** and **Janssen** for participation in advisory boards and educational workshops unconnected to the submitted work, and is also employed as expert scientist at **Roche Pharma Research** and Early Development; Roche Pharma was not involved in the work.*

*The University of Liverpool is the recipient of grant income from **Gilead**, **Janssen**, and **ViiV** for research projects of which AMG is the principal investigator.*

*PC reports personal fees from **Gilead**, **Janssen**, **Merck**, and **ViiV**.*

*AA reports grants and personal fees from **Bristol-Myers Squibb** and **Janssen-Cilag**; grants, personal fees, and non-financial support from **Gilead Sciences** and **ViiV Healthcare**; personal fees from **Merck**; and non-financial support from **AbbVie**.*

*AC reports personal fees and other from **Gilead Sciences** (conference travel bursaries and consultancy fees), and personal fees and other from **ViiV Healthcare** (conference travel bursaries and consultancy fees).*

*FR has received research funding or honoraria from or has consulted for **Gilead Sciences**, **Janssen**, **Merck**, **MSD**, and **ViiV Healthcare**.*

*JRB reports grants from **CHIP Copenhagen**, during the conduct of the study; and lecture honoraria from **AbbVie**, **Gilead**, **Merck Sharp & Dohme**, **ViiV**, **Hexal**, **Janssen**, and **Roche**.*

*GW reports grants from **Gilead Sciences** and **AbbVie**.*

*FG reports personal fees from **Janssen-Cilag**, **ViiV Healthcare**, and **Gilead Sciences**.*

*KB reports personal fees from **Viiv**, **Gilead**, **Merck**, and **Janssen**; and grants from **ViiV** and **Gilead**.*

*MK reports non-financial support from **Gilead Sciences**.*

*MR reports personal fees from **AbbVie**, **Gilead**, **GSK/ViiV**, **Janssen-Cilag**, and **MSD/Merck**.*

*HJ reports other support from **Gilead**, **Janssen**, and **ViiV**, during the conduct of the study.*

*H-JS reports personal fees and other support from **Gilead Sciences**, **Janssen-Cilag**, and **Merck Sharp & Dohme**; and other from **ViiV Healthcare**, **GlaxoSmithKline**, and **AbbVie**.*

All other authors declare no competing interests."

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*"**Unrestricted grant funding** was received from **ViiV Healthcare**, **Gilead Sciences**, **Augustinus Fonden**, and **A P Møller Fonden**."*

Shouldn't people be informed about these side effects of this ***independent research***? Or better not, because of the epidemic?

4.7. Summary: HAART and so called *HIV-related diseases*

The reported adverse effects of HAART match 1: 1 the so-called *HIV-related diseases*. That means the damages caused by the drugs are simply attributed to the putative HI virus.

It should be noted here that we do not speak of the so-called opportunistic infections (OI), i.e. infections that are favored by a malfunctioning immune system (*immunosuppressed*). These should, according to the theory, occur after about 10 years or more. However, this theory stems from a multiple infected and heavily drug infected population.

HIV-related diseases are putative diseases that occur earlier than OI but are also thought to be due to a supposed effect of HIV. However, these are only the side effects of the HAART *medication*.

We use the following definitions of HIV-related diseases and compare them to the reported side effects of HAART (see text):

Definitions of *HIV-related diseases*:

- Table 189-3, "*Conditions Associated with Persistent Immune Activation and Inflammation in Patients With HIV Infection*", aus Fauci, Lane, "*Human Immunodeficiency Virus Diesease: AIDS and Related Disorder*", in Longo et al., "*Harrisons Principles of Internal Medicine"*, 18ed., **2012**, p. 1526

and

- Lucas, Nelson, „*HIV and the spectrum of human disease.*", J Pathol. **2015** Jan;235(2):229-41, https://www.ncbi.nlm.nih.gov/pubmed/25251832

Definition according to:	**Supposed HIV-related symptoms = observed adverse effects of HAART**										
Fauci, Lane (2012)		Accelerated Aging Syndrome	Bone fragility	Cancers	Cardiovascular disease	Kidney disease	Liver disease	Neuro-cognitive dysfunction			
Lucas, Nelson (2015)					Cardiovascular diseases		Hepatic diseases	central nervous system diseases	Pulmonary dieseases		
Author	**Substance**									**Further adverse effects**	**Comments**

Richmann (1987)	AZT		x							macrocytosis, anemia, neutropenia, Bluttransfusionen erforderlich	
Seligmann (1994)	AZT							x		gastrointestinal symptoms, haematological toxicity, 6 dead	
Scruggs (2008)	AZT				x						Myopathy
Butanda-Ochoa (2017)	AZT						x				
Demir (2015)								x			
Caron (2008)	AZT	x									
Jones (2005)	d4T, AZT	x								lipoatrophy	
Schmitz (1994)	AZT								x	neutropenia, severe subjective symptoms	
Christensen (2017)	Abacavir/ Dolutegravir/ Lamivudine						x				
Haas (2015)	Abacavir/ Dolutegravir/ Lamivudine					x	x	x		rhabdomyolysis	
Di Filippo (2014)	Abacavir						x				
Calmy (2009)	boosted Protease Inhibitor		x			x					
Mallon (2005)	NRTI	x									
Payne (2011)	Nucleosid Analogs	x									Damage to the mitochondria
Fenaux (2016)	Nucleoside Inhibitors	x					x				Damage to the mitochondria
Schweinsburg (2005)	Didanosine, Stavudine	x						x			Damage to the mitochondria
Stauch (2017)	Efavirenz, Nevirapine, Abacavir, Emtricitabine, Zidovudine, Darunavir, Lopinavir, Raltegravir, Maraviroc	x						x			Damage to the mitochondria
Kakuda (2000)	NRTI	x	x		x	x	x	x		lipodystrophy, diabetes, lactic acidosis	Damage to the mitochondria
Moyle (2000)	NRTI	x			x			x	x	lipodystrophy	Damage to the mitochondria
Patel (2004)	Nevirapine						x			fever, skin rash, eosinophilia	In-vivo, HIV-negative persons
Hitti (2004)	Nelfinavir or Nevirapine with Zidovudine plus Lamivudine						x			Stevens-Johnson syndrome	Study suspended because of adverse effects
Bertrand (2016)	Efavirenz, Etravirine, Rilpivirine and Nevirapine							x			cerebrovascular pathology
Taiwo (2006)	Nevirapine						x				
Sastry (2018)	Nevirapine						x			skin rash	

Paemanee (2017)	Nevirapine	x					x				Damage to the mitochondria
Tseng (2014)	nevirapine plus two nucleos(t)ide reverse-transcriptase inhibitors.						x			skin rash	
Mukherjee (2017)	Zidovudine, Tenofovir, Nevirapine, Efavirenz, Atazanavir						x	x		anemia, gastrointestinal side effects	
Birbal (2016)	Stavudine, Efavirenz, Zidovudine, Nevirapine and Tenofovir							x		lipodystrophy, skin rash, anaemia and hyperlactatemia, gynaecomastia	
Harris (2008)	Raltegravir, Efavirenz, Lopinavir, Ritonavir , Atazanavir, Nevirapine, Stavudine							x		gastrointestinal intolerance, auditory hallucinations, poor sleep, lack of energy,	
de Boer (2016)	Dolutegravir							x		Insomnia and sleep disturbance, gastrointestinal complaints	
Brooks (2018)	Dolutegravir, Isoniazid, Rifapentine									flu-like syndrome	Studie stopped
Santoriello (2017)	Atazanavir					x					
Hirakawa (2017)	Protease Inhibitors, Integrase Strand Transfer Inhibitor-containing regimen		x								
Muhammad (2017)	HAART, Protease Inhibitors containing regimen				x					Metabolic Syndrom (MS): central obesity, high blood pressure, high blood sugar,	
Ascher (1997)	Indinavir					x				fever, chills, nausea, vomiting, decreased appetite, sterile pyuria, nasal congestion	
Roland (1997)	Indinavir					x					
McLaughlin (2018)	Atazanavir, Indinavir, Abacavir, Didanosine, Lamivudine, Stavudine, Efavirenz, Rilpivirine, Enfuvirtide, Dolutegravir and Raltegravir					x				crystalluria, leukocyturia, nephritis, nephrolithiasis, nephropathy and urolithiasis, nephropathy, renal failure, nephritis, proteinuria, renal stones	
Loens (2018)	Zalcitabine, Stavudine Didanosine, Indinavir	x			x	x				organ accelerated ageing and of an increased vascular risk	
McMahon (2018)	long-term treated HIV									diabetes	
Friis-Møller (2003)	Protease Inhibitor (PI) Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)				x						

Wand (2007)	ART				x					metabolic syndrome (MS), type 2 diabetes mellitus	
Ekoru (2018)	ART				x						
Carr (1998)	Protease Inhibitors, Ritonavir, Saquinavir				x					lipodystrophy, hyperlipidaemia, diabetes mellitus	
Nansseu (2017)	HAART				x					lipodystrophy, prediabetes and overt diabetes, insulin resistance and hyperlactatemia/lactic acidosis	
Tsai (2017)	ART				x				x	hyperlipidemia, diabetes	
Torres (2014)	ART, NRTI	x									
Lipshultz (2011)	ART				x						
Hoy (2017)	ART		x								
Carr (2015)	ART		x								
Grund (2009)	ART		x								
Tebas (2000)	Protease Inhibitor, ART		x								
Bernardino (2015)	Darunavir, Ritonavir, Raltegravir, Tenofovir, Emtricitabine		x								
Brown (2015)	Tenofovir Disoproxil Fumarate, Emtricitabine, Atazanavir Ritonavir, Darunavir, Raltegravir		x								
Cook (2016)	Tenofovir Disoproxil Fumarate, Efavirenz, Emtricitabine, Ritonavir, Darunavir, Raltegravir		x								
McComsey (2011)	Abacavir-Lamivudine, Tenofovir Disoproxil Fumarate-Emtricitabine, Efavirenz, Atazanavir-Ritonavir		x								
Assoumou (2013)	cART		x								
Gafni (2006)	Tenofovir Disoproxil Fumarate		x								
Grigsby (2010)	Tenofovir		x								Partial recovery of bone density after discontinuation of TDF
Grant (2016)	Tenofovir		x								
Borges (2017)	ART			x							
Crum-Cianflone (2010)	ART			x							non-AIDS-defining cancers
Piketty (2008)	ART			x							anal cancer

Mayor (2008)	HAART			x							non-AIDS-defining lymphomas, prostate carcinoma, and cervical carcinoma
Bower (2003)	HAART			x							lung cancer
Engels (2006)	HAART			x							lung cancer
Lee (2016)	ART			x							
Tetteh (2017)	Emtricitabine, Tenofovir		x			x	x	x		hypophosphatamia, proteinaemia, glucosuria, pancreatitis, lactic acidosis, flu-like symptoms, hypertriglyceridemia, increased creatinine phosphokinase, unusual dreams, hyperpigmentation	
Reisler (2003)					x		x				
John Holloway	ART	x	x	x				x	x		
Scott Jordan	ART	x								No further data	13 different medications daily
James Malone, Hayward, CA, USA: HIV-	ART	x								No further data	HIV-, misdiagnosis, treated for 20 medical conditions
Bobby Russell, Lexington, KY, USA: HIV-	ART									No further data	HIV-, misdiagnosis taking up to 15 pills a day
Farida Kiconco, Sheema, Uganda: HIV-	ART						x		x	No further data	HIV-, misdiagnosis
Peter Mungai Njoroge, Nairobi, Kenya: HIV-	ART							x		No further data	HIV-, misdiagnosis

The principle is simple: everything in which cells have to divide is affected. However, we look at Scott Jordan (HIV+ measured) with 13 different *medications*, Bobby Russell and James Mallone (**both HIV-**) with 15 and 20 different *medications*, respectively, and ask us, what is being treated and where is the disease?

When we look at the official website of the NIH in the USA, we find all HIV-related diseases listed as adverse effects of ART. It should be noted that adverse effects are attributed to different types of medication, see Table 15 - *Common and / or Severe Adverse Effects Associated with Antiretroviral Therapy*. However, HIV+ measured people usually do not take a single drug, but a cocktail of mostly 3 sometimes 4 or 5 drugs

(HAART). In addition, the medication is changed sometimes due to the adverse effects so that the individual is exposed to different adverse effects over time (= the rest of the remaining life!).

Similarly, we find agreement with the adverse effects in ***HIV-neg., msdiagnosed people***.

- NIH, "*Adverse Effects of Antiretroviral Agents*", Oct 25, **2018**, https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/31/adverse-effects-of-antiretroviral-agents

Adverse Effects (*Summary from Table 17 - Common and/or Severe Adverse Effects Associated with Antiretroviral Therapy*):

(Highlighted are adverse effects, which correspond to the so-called *HIV-related diseases*)

Bleeding Events
Bone Density Effects
Bone Marrow Suppression
Cardiac Conduction Effects
Cardiovascular Disease
Cholelithiasis
Diabetes Mellitus and Insulin Resistance
Dyslipidemia
Gastrointestinal Effects
Hepatic Effects
Hypersensitivity Reaction
Excluding rash alone or Stevens-Johnson syndrome
Lactic Acidosis
Lipodystrophy
Myopathy/Elevated Creatine Phosphokinase
Nervous System/Psychiatric Effects
Rash
Renal Effects/Urolithiasis
Stevens-Johnson Syndrome/Toxic Epidermal Necrosis

Who should survive this? Nobody. HIV/AIDS is just a deadly disease.

For the ***non-HIV co-morbidity*** of HIV+ people under antiretroviral therapy (ART) cf. also the following study,

- Maggi et al., "*Clusterization of co-morbidities and multi-morbidities among persons living with HIV: a cross-sectional study.*", BMC Infect Dis. **2019** Jun 25;19(1):555, https://www.ncbi.nlm.nih.gov/pubmed/31238916

"Non-HIV co-morbidities included: ***cardiovascular disease, diabetes mellitus, hypertension, oncologic diseases, osteoporosis****, probable case of chronic obstructive pulmonary disease (COPD), hepatitis C virus (HCV) infection,* ***psychiatric illness, kidney disease****."*

"Table 1 - Characteristics of 1087 patients enrolled in the Cluster Project: ***Years since ART initiation 9.0*** *(4.0–16.0)"*

*"The most frequent co-morbidity was **dyslipidemia** (55.3%), followed by **hypertension** (31.4%), COPD (29.4%), hepatitis C virus (HCV) infection (25.4, 5.5% with detectable HCVRNA), **psychiatric illness** (10.3%), diagnosis of **osteopenia/osteoporosis** (10.1%), **diabetes** (6.1%), and **renal impairment** (4.8%); 95 (8.7%) subjects had history of **non-AIDS-defining cancer**. Forty-nine patients (4.5%) had **pCVD events**."*

*"Our data evidence that, in spite of mean age lower than 50, **co-morbidity was the rule among our PLWH (82%), and that more than 50% of our patients were multi-morbid**. Moreover, about 30% of them had three or more chronic non-HIV related conditions, thus confirming recent data provided by other studies in the field."*

The match of the known adverse effect with these co-morbidities is ***1:1***.

In view of the severe side effects described, "*generally well-tolerated*" cannot be a description of HAART. This is undoubtedly demonstrated by the cases of misdiagnosed persons.

This match of severe side effects of HAART with so-called *HIV-related diseases* is certainly no coincidence. Where is the publication that systematically investigates this?

While people suffer from the severe side effects of the therapy, science ***speculates*** about an increased level of inflammation in people measured with HIV, cf.

- Pamela Dörhöfer, „*HIV und Aids: Kampf gegen die Stigmatisierung – Interview mit Jürgen Rockstroh, Präsident der Europäischen HIV/Aids-Gesellschaft*", 19 Nov **2019**, https://www.fr.de/wissen/hiv-aids-kampf-gegen-stigmatisierung-13201336.html

„Liegen bereits Erkenntnisse vor, ob eine langjährige Infektion und Einnahme der Tabletten verstärkt zu bestimmten Begleiterkrankungen führen?

*Es gibt verschiedene Forschungsprojekte, die sich mit dieser Frage beschäftigen. Wir wissen, dass **Bluthochdruck**, **Diabetes Mellitus** und **Osteoporose** häufiger und bereits in jüngerem Lebensalter auftreten. Das hängt **vermutlich** damit zusammen, dass bei Infizierten – auch wenn sie mit Medikamenten die Viruslast gering halten – das Immunsystem ständig stimuliert wird. Das löst eine Entzündungsreaktion aus, die all diese Erkrankungen begünstigt."*

[Translation: *HIV and AIDS: Fighting Stigmatization - Interview with Jürgen Rockstroh, President of the European HIV/AIDS Society*]

"Are there any findings as to whether a long-term infection and taking the tablets lead additionally to certain concomitant diseases?

*There are various research projects dealing with this question. We know that **high blood pressure**, **diabetes mellitus** and **osteoporosis** occur more frequently and at a younger age. This is **presumably** due to the fact that in infected people - even if they keep the viral load low with medication - the immune system is constantly stimulated. It triggers an inflammatory reaction that favors all these diseases."*

That would be an amazing variety of diseases for one single pathogen, which is neutralized by antibodies and in contrast to *opportunistic infections* that should occur after 10-15 years (*slow virus*). We are not aware of one other pathogen with this diversity and which in addition becomes ***chronic in 100% of the cases in therapy***, and this for all ages, all races and both sexes.

It looks like Mr. Rockstroh's presumption is not correct. It is due to the putative antiretroviral substances, whose side effects match ***1:1*** the co-morbidities described.

The question may be whether someone with 12 *conflicts of interest* is actually independent enough to judge, or better, to ***presume*** in this important matter. But there is the opportunity for further therapies whose dependencies are being researched intensively.

The question is what extent the complexity of standards, methods, procedures, tests, therapies, etc. created by science itself and the resulting dependencies between diagnoses, morbidities and presumed medication actually contribute to the clarification of this matter.

If you look at the guidelines of the *European HIV/AIDS Society*, it becomes clear that a whole universe of diagnoses, therapies, presumed medications and interactions between them has emerged in the wake of HIV (*not AIDS*!), cf.

- Europeanv AIDS Clinical Society, "EACS Guidelines 2019", https://www.eacsociety.org/files/2019_guidelines-10.0_final.pdf

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The number of dependencies is in the thousands, maybe tens of thousands. How many of these *drug-drug interaction* studies have been performed on ***HIV+ measured human beings*** and what were the consequences?

But in these data universes it is easy to ***presume***. Only the obvious has no place there.

Where is the much praised evidence-based medicine (EbM)? Or is it more *a willing-to-notice-based medicine* (WbM)?

However, without these *HIV-related diseases*, we are back at the *slow virus* concept and the effects of a putative pathogen after 10-15 years with completely symptom-free years, for people who are not otherwise ill, in between. The fairy tale of HIV-related diseases is supposed to relativize the adverse effects on the one hand and to make it plausible that there is even an effect of the putative virus on the other hand.

However, it is the sign of a failed theory. Un-thinkable is not un-human.

We return to the topic of HAART in connection with nitrites and oxidative cell stress below.

5. Physicians and basic biochemical research

It is opportune to look at the role of physicians in biomedical sciences, and it is instructive to begin with the *HIV Buch* edited by Hoffmann and Rockstroh, cf. https://www.hivbuch.de/wp-content/uploads/2017/04/hiv2016-17_fix.pdf

Nobody says that doctors do not want to help and there are enough responsible doctors. However, it seems, and so it can be read in my opinion in the introduction to the *HIV Buch,* that after the first 5 AIDS cases in San Francisco in the early 1980s, panic broke out as nobody had any idea what they were dealing with. In the following years more patients were affected by AIDS-defining diseases, at the time almost 100% in the US homosexual community, which at that time was marked by heavy drug use. Here especially "*Poppers*" as an aphrodisiac and a nitrite-containing substance, cf.

- John Lauritsen, Hank Wilson, "*Death Rush: Poppers and AIDS*", **1986**

http://paganpressbooks.com/jpl/POPPERS.HTM

„*96-100% of the gay men with AIDS used poppers, usually quite heavily*." (page 10)

The HIV book is authored by physicians and the first part of the book addresses the historical context of the epidemic and possible viral causes. The text in the first part (basics) seems cumbersome and fuzzy.

This changes abruptly and the words flow in the second part, when it comes to therapies, drugs, drug resistance, drug interactions, laboratory values and so on. Especially when it comes to the diagnosis of AIDS catalog diseases, cf. WHO, "*Overview of Internationally Used HIV / AIDS Case Definiti*ons", http://www.who.int/hiv/strategic/surveillance/definitions/en/ or corresponding differential diagnoses and interactions, between diseases, between medications, etc.

Here the physician is at home, here he can work his medical program. These procedures have largely taken a life of their own. The interest seems to be above all the question of whether the health insurance companies and thus the general public takes over the costs of the very expensive diagnostic procedures and medicines.

But, would it not have been desirable to sharpen the basics a bit before? For example, the questions from *Coffin* and *Swanstrom*, see above?

The open questions about the basics are often unknown to treating physicians. Their role is more or less passive. Which treating doctor maintains his own laboratory and does his own basic research?

Here one seems to rely on the other. Physician on biologists and pharmacists, biologists on physicians, pharmacists on toxicologists, biochemists on laboratories, the state on industry, industry on research and research again on physicians. In basic research everybody sits in front of his or her molecule and publishes. It is hardly noticed that, according to the original statistics, we should have all been dead long ago and / or had to climb over corpses of dead female prostitutes. Part of the reason I see lays in the over-reliance of physicians on laboratory values. Values, which they can hardly understand themselves. Here we mention in advance PCR and its pseudo accuracy. Hardly any doctor is aware of how enormously complicated a mammalian cell is.

Especially in the relationship of physician and laboratory, the open questions about the theory have too quickly given way to a wrong diagnostic routine, which, however, only works within a narrow framework, cf.

- Hoffmann und Rockstroh, „*HIV-Buch*“, **2017**, https://www.hivbuch.de/wp-content/uploads/2017/04/hiv2016-17_fix.pdf (p. 137)

„***Praktische Hinweise im Umgang mit Viruslast und CD4-Zellen***

…

*Möglichst bei einer Messmethode (**im gleichen Labor**) bleiben – methodisch bedingte Schwankungen (bis zu einer halben Logstufe) berücksichtigen!*

…“

Translation

“***Practical information in dealing with viral load and CD4 cells***

…

*If possible, stay with a measuring method (**in the same laboratory**) - take into account methodical variations (up to half a log level)!*

…“

As of 2017.

An objective theory and methodology would hardly depend on the laboratory. The desire of medicine to find in molecular diagnosis (*à la PCR*) an objectification of the diagnosis process with all its problems and difficulties has not come true. The section that one looks at on a molecular level is much too small to get a holistic picture of the affected person.

How to deal with the occurring contradictions? They are attributed to the putative virus that mutates too fast. Cf.

- Eberle, Pauli-Volkert, „*Wie zuverlässig ist die Viruslast-Bestimmung?* “, HIV & more, 04/**2008**, https://www.hivandmore.de/archiv/2008-4/HIVm4_08_AktEberle.pdf

*„Allerdings ist bei der **hohen Variabilität von HIV in extremen Einzelfällen** **mit einer Fehlbestimmung oder sogar einem Ausfall eines Verfahrens zu rechnen**.“*

Translation

*"However, with the **high variability of HIV in extreme individual cases** an incorrect determination or even a failure of a procedure is to be expected."*

What does *extreme individual cases* mean? This is stated in the text as follows, ibid.

„In dieser Studie sind acht von 170 Patienten aufgefallen, bei denen die Viren mit einem Testverfahren entweder gar nicht oder deutlich zu niedrig gemessen worden waren.“

Translation

"In this study, in eight out of 170 patients the viruses using one test procedure were measured either not at all or clearly too low. "

8 out of 170, that would be about 5%. This does not sound like *extreme individual cases*, but like *appeasement*, by ad hoc assumptions for which there is no evidence. The alleged results are interpreted only in the direction of the *scientific consensus*. Objective science looks different.

The contradictions that this conjecture on the very one-sided effects of mutations causes will be discussed again below[4]. In addition, the question arises as to which other factors influence PCR in the often multiply (classically) infected risk groups, see below.

Everything is based on the 20-40 base pairs of the PCR primers (see below) that have been declared as representative of the virus and entries in the gene databases that are so numerous that it can be used to construct several thousand complete genomes of the putative HI virus (see below).

But, a doctor today has no other option than to treat HIV according to the "*rules of the best medical practice.*" That means HAART. He would otherwise be punishable. The same applies to delivery by an HIV+ measured mother. If the mother refuses to have a corresponding HIV therapy for the child, the child is taken away from her. Everything else would completely run against the present "*rules of the profession*".

However, the mother and her child are light years away from the original AIDS population, highly drug addicted, gay men with changing sexual partners and frequent unprotected anal intercourse.

But can one hold a chemical (possibly medical) cause for a virus epidemic? One can.

[4] This refers to the question, why every mutation of this supposedly rapidly mutating organism should lead to a pathogen, so in each case (= 100%) makes sick, despite mutation.

6. SMON (Japan 1955 – 1971)

It is often overlooked, but the tragedy of the SMON crisis in Japan was not only the drug scandal, but that for more than 10 years, an epidemic was assumed to be caused by an unknown and never found infectious agent.

Jeanne Lenzer**, „***When a Medical "Cure" Makes Things Much, Much Worse*", 02 Jan **2018**, https://www.smithsonianmag.com/science-nature/when-cure-is-cause-180967666/

„The illusion that SMON was an infectious disease was compelling"

From the article on SMON epidemic between about 1955 and 1971 by Jeanne Lenzer we can learn two things:

a) It is possible to hold a drug scandal for more than 10 years for a viral epidemic.
b) There is almost no independent research in the US today.

Here is the statement from 1971, more than 10 years after the outbreak of the alleged epidemic, that there is a virus:

- Inoue et al., "*Virus associated with S.M.O.N. in Japan*", Lancet, 24. April **1971**, p. 853-854, https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(71)91513-3/fulltext?code=lancet-site

*"Studies on the pathogenicity of the virus in mice suggest that **the virus is a new neuropathic slow virus**; the pathological findings include spongy degeneration in the brain. Further investigations about the properties of the virus are now in progress."*

And here's the statement, 4 years later that the experiment that claimed to have found the virus could not be confirmed.

- Yoshino et al. "*Failure to Reproduce the Cytopathic Effect and Chorioallantoic Membrane Reactions of the so-called SMON Herpesvirus*", Japan. J. Microbiol.Vol. 19 (5), 407-410, **1975**, https://www.jstage.jst.go.jp/article/mandi1957/19/5/19_5_407/_article/-char/en

Likewise,

- Kono, "*The S.M.O.N. Virus Theory*", Lancet, August 23, **1975**, p. 370-371, https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(75)92818-4/abstract?code=lancet-site

*"Inoue et al. published several papers on S.M.O.N. (subacute myeloopticoneuropathy) virus (Inoue agent), and **a standard textbook adopted Inoue's virus theory as confirmed**. However, research in the laboratories of the S.M.O.N. Research Commission in Japan **failed to confirm Inoue's results**."*

*"The annual incidence of S.M.O.N. in Japan of **fell dramatically after the banning of sales clioquinol** from Sept. 8, 1970. […] If the virus is shed at a high rate, as shown by Inoue, irrespective of stage of the illness, the chain of infection must continue and S.M.O.N. must arise as before. **Our conclusion is that Inoue agent cannot be regarded as the etiological agent of S.M.O.N.**"*

7. Zoonosis 1910 – 1950

According to the actual theory, various SIV virus have passed around 1930 in Africa at least 7x by zoonosis from monkeys (SIV) to humans (HIV), cf.

- Hahn et al. "*AIDS as a zoonosis: scientific and public health implications*.", Science. **2000** Jan 28; 287(5453):607-14, https://www.ncbi.nlm.nih.gov/pubmed/10649986

"*Evidence of simian immunodefciency virus (SIV) infection has been reported for 26 different species of African nonhuman primates. Two of these viruses, SIVcpz from **chimpanzees** and SIVsm from **sooty mangabeys**, are the cause of acquired immunodefciency syndrome (AIDS) in humans. Together, they have been transmitted to humans **on at least seven occasions**."*

*"How the AIDS epidemic actually began, what the contributing factors were, and **why it appeared in the mid- to late 20th century (and not before) are not known**. Whatever the final answers are, they must account for*

(i) at least seven separate introductions of SIVcpz and SIVsm viruses into humans;
(ii) the fact that the HIV-1 group M, N, and O viruses are significantly more closely related to SIVcpz viruses from P. t. troglodytes than to the single SIVcpz isolate from P. t. schweinfurthii; and
*(iii) **the estimation of 1930 (range 1910 to 1950) as the timing of the last common ancestor of the HIV-1 group M viruses.**"*

Between 1910 and 1950, SIV is said to have jumped in Africa over at least ***7x*** to humans. Meanwhile recent publications speak of ***13x*** transitions between species, cf.

- Peeters et al., „*Origin and diversity of human retroviruses*.", AIDS Rev. **2014** Jan-Mar;16(1):23-34, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4289907/

*"More in detailed studies showed that SIVs from chimpanzees and gorillas have crossed the species barrier on at least **four** occasions leading to HIV-1 group M, N, O and P in humans [6,23]. The different HIV-2 groups are the result from at least **nine** independant transmissions of SIVs from sooty mangabeys in west Africa [6,23,24]."*

And the number of zoonoses is likely to grow, cf. ibid,

*"**Already 13 transmissions involving 3 different NHP species to humans have been documented, 4 for HIV-1 and 9 for HIV-2.** Most likely other cross-species occurred in the past but remained undetected, because the virus could not adapt to his new host or was not introduced into an environment where conditions for efficient and rapid spread were present. Today humans are still exposed to a wide diversity of SIVs through hunting and butchering NHPs for bushmeat."*

The alleged ***13-fold*** jump across the species boundary around ***1930*** comprises the jump from chimpanzees (SIVcpz) and gorillas (SIVgor) to humans forming the HIV-1 groups, with the most widespread group M, and from sooty mangabeys (SIVsmm) to humans, with the formation of the HIV-2 groups, which outside of the

West -Africa almost do not occur. That is the theory, although SIV does not induce diseases in apes and monkeys (non-pathogenic), see below for the animal model.

Before 1910 is not possible, otherwise there would have been an epidemic earlier. Later than 1950 is not possible due to the > 10 years of latency of *slow virus* and the first cases in 1981 in the USA, see below.

According to the theory, at the same time, 2 different pathogenic HI virus groups have formed, HIV-1 and HIV-2, differing by > 45% in their genome, cf.

- Motomura et al., "*Genetic Recombination between Human Immunodeficiency Virus Type 1 (HIV-1) and HIV-2, Two Distinct Human Lentiviruses*", J Virol. **2008** Feb; 82(4): 1923–1933, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2258735/

"HIV-1 and HIV-2 have similar genetic structures; however, they exhibit significant sequence variation. For example, ***the two virus strains used in this study contain only 55% nucleotide sequence identity*** *in the viral genome and 54%, 55%, and 35% amino acid sequence identity in* gag, pol*, and* env*, respectively."*

That seems a bizarre coincidence. And there is not the slightest proof of this. One could also ask, how evolution ever got this far in the face of this threat scenario.

But it is the time from about 1960, when the electron microscopes and antibody tests became available. And then later PCR. Fortunately, the disease-defining apparatus (*PCR viral load*) was developed at the same time as the disease was discovered!

It is also the time when modern drugs came into use.

The hands smeared with monkey blood, that Hahn et al. show (in color!) have no significance, but serve as a colorful background of a weak theory. One overlooks deliberately the question of what happened during the 200,000 years before.

Concerning this question Hahn et al. simply state: „*To account for the appearance of AIDS as an epidemic in the 20th century, and not before, a combination of various contributing factors has been proposed: social disruption, enslavement, urbanization, prostitution, and other sociobehavioral changes* ***not yet fully understood.***"

Cf. the **textbook** "*Medical Microbiology*", Jawetz, Melnick and Adelberg, 26th Edition, **2013**, p. 656:

"*Origin of AIDS – HIV in humans originated from cross-species infections by simian viruses in rural Africa, probably due to direct human contact with infected primate blood. Current evidence is that the primate counterparts of HIV-1 and HIV-2 were transmitted to humans in multiple (****at least seven****) different occasions. Sequence evolution analyses place the introduction of SIV$_{cpz}$ into humans that gave rise to HIV-1 group M* ***about 1930****, although some estimates push the date back to about 1908. Presumably, such transmissions occurred repeatedly over the ages,* ***but particular social, economic, and behavioral changes that occurred in the mid 20th century provided circumstances that allowed these virus infections to expand****, become well-established in humans, and reach epidemic proportions.*"

Strangely, the SI virus (simian immunodeficiency), the non-pathogenic homolog in monkeys, has existed for more than 32,000 years, cf.

- Worobey et al., "*Island biogeography reveals the deep history of SIV*.", Science **2010** Sep 17;329(5998):1487, https://www.ncbi.nlm.nih.gov/pubmed/20847261/

*"Our phylogeographic approach establishes that SIV is ancient and **at least 32,000 years old**. Our conservative calibration point and analyses of gene sequence saturation and dating bias **suggest it may be much older."***

There was plenty of time for zoonosis. Why should a deadly virus have been created around 1930? The zoonosis data does not give the slightest hint („*… and other sociobehavioral changes **not yet fully understood***.")

It is also ignored that monkeys do not develop AIDS (see below), as well as cats, horses, goats, sheep or cows. "*AIDS-like*" symptoms in monkeys can only be generated in special cases with specially adapted viruses.

TABLE 44-2 Representative Members of the *Lentivirus* Genus

Origin of Isolates	Virus	Diseases
Humans	HIV-1 (SIV_{cpz})[a] HIV-2 (SIV_{sm})	AIDS
Nonhuman primates[b]		
Chimpanzee	SIV_{cpz}	Simian AIDS
Sooty mangabey	SIV_{sm}	
Macaques[c]	SIV_{mac}	
African green monkey	SIV_{agm}	
Sykes monkey	SIV_{syk}	
Mandrill	SIV_{mnd}	
l'Hoest monkey[c]	SIV_{lhoest}	
Colobus monkey	SIV_{col}	
Nonprimates[d]		
Cat	Feline immunodeficiency virus	Feline AIDS
Cow	Bovine immunodeficiency virus	
Sheep	Visna/maedi virus	Lung, central nervous system disease
Horse	Equine infectious anemia virus	Anemia
Goat	Caprine arthritis encephalitis virus	Arthritis, encephalitis

[a]The origins of HIV-1 and HIV-2 were cross-species transmissions of SIV_{cpz} and SIV_{sm}, respectively.

[b]Disease not caused in host of origin by SIVs but requires transmission to a different species of monkey (rhesus are the most susceptible to disease). The Asian macaques (rhesus) show no evidence of SIV infection in the wild; SIV_{sm} was probably accidentally introduced to macaques in captivity.

[c]Indention indicates that the virus is in the same phylogenetic lineage as the one above it.

[d]Nonprimate lentiviruses cause disease in species of origin.

*(Overview of presumed lenti viruses. From "Medical Microbiology", Jawetz, Melnick and Adelberg, 26th Edition, **2013**, p. 656.)*

Caution should be exercised here because the latency period of these "*slow virus*" or "*lentiviruses*" is in the range of the natural life expectancy of healthy animals.

What should be discussed, however, is why the widespread prevalence of suspected immunosuppressive viruses in the animal kingdom according to the current theory has not led to a pathogenic virus in humans much earlier? Domesticated cats, goats, sheep, cattle and horses have coexisted with humans for several thousand years, also in Europe. From the point of view of evolution, too, it is extremely unlikely that these retroviruses are so widespread but are said to have only occurred in humans for a few decades.

And sheep, goat, beef and horse meat has also been consumed in Europe for several thousand years. And why should a zoonosis in Africa first cause an epidemic in the US? This is another indirection to explain.

Further references,

- Forsman, Weiss, "*Why is HIV a pathogen?*", Trends Microbiol. **2008** Dec;16(12):555-60, https://www.ncbi.nlm.nih.gov/pubmed/18977141

"Comparative studies of lentivirus infections in other species show that AIDS is not an inevitable outcome of infection ***because simian immunodeficiency virus in natural hosts seldom causes disease****."*

On HIV-2 cf.

- Dunham et al., "*The AIDS resistance of naturally SIV-infected sooty mangabeys is independent of cellular immunity to the virus*.", Blood. **2006** Jul 1;108(1):209-17. Epub 2006 Mar 7, https://www.ncbi.nlm.nih.gov/pubmed/16522814

"These findings indicate that the ***absence of AIDS in naturally SIV-infected sooty mangabeys*** *is independent of a strong cellular immune response to the virus."*

Where are the mountains of dead apes and monkeys in the jungle, which have died of *AIDS-like symptoms*?

Maybe something is fundamentally wrong with the concept of "*slow virus*" (lentiviruses) and the 10-20 years latency?

In addition, there is the fact that other mammals, mice and dogs, respond positively to HIV serum tests, even though they had never been exposed to the HIV virus, cf.

- Kion et al. "*Anti-HIV and anti-anti-MHC antibodies in alloimmune and autoimmune mice*.", Science **1991** Sep 6;253(5024):1138-40, https://www.ncbi.nlm.nih.gov/pubmed/1909456

"Alloimmune mice (mice that have been exposed to cells from another murine strain) were shown to make antibodies against gp120 and p24 of human immunodeficiency virus (HIV), and mice of the autoimmune strains MRL-lpr/lpr and MRL-(+)/+ made antibodies against gp120. ***This is surprising because the mice were not exposed to HIV***."

- Strandstrom et al. "*Studies with canine sera that contain antibodies which recognize human immunodeficiency virus structural proteins*.", Cancer Res. **1990** Sep 1;50(17 Suppl):5628S-5630S, https://www.ncbi.nlm.nih.gov/pubmed/2386966

"In a serological survey, using the immunoblotting technique, we found that substantial numbers of dog sera from both normal and diseased dogs, including dogs with neoplasia, reacted with one or more human immunodeficiency virus (HIV) recombinant proteins. ***A total of 144 dog sera were tested, and 72 (50%) of them reacted with one or more HIV recombinant structural proteins****."*

"The origin of lentiviruses has not yet been established. Our results are provocative, although not conclusive, ***suggesting the possibility that dogs might be an important link in our understanding of interspecies lentivirus relatedness*** *and perhaps of their pathogenesis."*

There is some evidence that the retroviral activities to be attributed to a putative HIV virus have long been part of the evolution of mammalian cells, and therefore humans cells as well. Why should South American indigenous peoples who do not develop AIDS otherwise be tested positive for HIV? Cf.

- Rodriquez et al. "*Antibodies to HTLV-III/LAV among aboriginal Amazonian Indians in Venezuela*" Lancet, Vol 326, ISSUE 8464, P1098-1100, Nov 16, **1985**, https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(85)90688-9/abstract

"*Serum samples from 224 aboriginal Amazonian Indians were tested for antibodies to HTLV-III/LAV by an indirect immunofluorescence (IF) assay. 9 individuals (4%), 5 of them female, were seropositive by IF and by confirmatory western blotting and radioimmunoprecipitation tests.*"

"*None of 211 randomly chosen, healthy blood donors from Venezuelan cities had antibodies to HTLV-III/LAV. The prevalence of specific antibodies among Amazonian Indians suggests the HTLV-III/LAV or a* ***closely related cross-reactive virus may be endemic in this area."***

Neither mice nor dogs nor Amazon Indians develop AIDS. AIDS in the sense of the catalog diseases of the WHO is developed especially by strongly drug-dependent homosexuals with numerous classical infections, thus the original AIDS population (see also below, Appendix III, on the composition of so-called HIV risk groups).

It seems much more plausible that the available data is read in a way only to support a very weak theory. It was important that in the end a virus results. But that is far from being the only explanation, as shown below.

8. Missing animal model - apes do not get AIDS

That the animal models for HIV do not work has been stated many times, i.e. there is no evidence of analogous processes with respect to virulence, pathogenesis, genetics, proteins, infection and host response.

There is no animal model of HIV and / or AIDS in animals, although this is has been claimed in vaccine research. That's not true, cf.

- Akhtar, "*The Flaws and Human Harms of Animal Experimentation*", Camb Q Healthc Ethics. **2015** Oct; 24(4): 407–419, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4594046/

"***HIV/AIDS vaccine research using NHPs represents one of the most notable failures in animal experimentation translation***. *Immense resources and decades of time have been devoted to creating NHP (including chimpanzee) models of HIV. Yet all of about 90 HIV vaccines that succeeded in animals failed in humans."*

- Shedlock et al., „*Monkeying around with HIV vaccines: using rhesus macaques to define 'gatekeepers' for clinical trials*", Nat Rev Immunol. **2009** October ; 9(10): 717–728, https://www.ncbi.nlm.nih.gov/pubmed/19859066

„*The major limitation surrounding HIV study in animal models is that* ***the virus does not replicate in most animal species tested****, including rodents and non-human primates (the rare exceptions being gibbon apes and chimpanzees; however, in these animals* ***HIV-1 infection is typically not associated with clinical diseases and haematological abnormalities****). Although chimpanzees are the closest species in evolutionary terms to humans, they are endangered, they are costly to maintain and their use can be of ethical concern. Thus, the focus has shifted* ***to viral surrogates of HIV, simian immunodeficiency viruses (SIVs),*** *for which infection in natural non-human primate hosts, such as sooty mangabeys and African green monkeys, is* ***generally non-pathogenic****, but experimental infection of non-natural hosts, such as Asian monkey species, including rhesus macaques (Macaca mulatta), results in the development of* ***disease similar to that described in patients with AIDS*** *(simian AIDS).*"

- Hatziioannou und Evans, „*Animal models for HIV/AIDS research*", Nat. Rev. Microbiol. **2012** December; 10(12): 852–867, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4334372/

„*One of the major limitations in searching for cures and vaccines for HIV-1 has been the lack of an animal model that recapitulates all of the salient features of HIV-1 infection in humans. HIV-1 is a direct descendant of SIVcpz, a virus that infects Central Africa chimpanzees (Pan troglodytes troglodytes) and might have a substantial impact on wild chimpanzee communities.* ***Nevertheless, HIV-1 infection of chimpanzees in captivity rarely results in the development of disease.***"

- Sharma, „*Exploring Experimental Animal Models in HIV/AIDS Research*", Biochem Anal Biochem **2013**, 2:2, https://www.omicsonline.org/exploring-experimental-animal-models-in-hivaids-research-2161-1009.1000129.pdf

„The animal relative closest to humans, the chimpanzee, had been exploited extensively in AIDS research, but it was realized off late ***that even chimpanzees do not develop human AIDS-like symptoms****.*“

„Rhesus macaque/SIV model has not contributed much to the development and optimization of AR therapy, because of their unsuitability.“

- Bailey , “*Assessment of the role of chimpanzees in AIDS vaccine research.*”, Altern Lab Anim. **2008** Sep;36(4):381-428, https://www.ncbi.nlm.nih.gov/pubmed/18826331

“***Vaccine responses in chimpanzees and humans are highly discordant.*** *Claims of the importance of chimpanzees in AIDS vaccine development are without foundation, and a return to the use of chimpanzees in AIDS research/vaccine development is scientifically unjustifiable.*”

“This analysis expands on previous data that underlined the ***poor performance of chimpanzees as models in HIV/AIDS research****, evidenced by a large number of negative opinions and comments toward it and by the significant withdrawal of NIH funding for it.”*

- Forsman, Weiss “*Why is HIV a pathogen?*”, Trends Microbiol. **2008** Dec;16(12):555-60, https://www.ncbi.nlm.nih.gov/pubmed/18977141

“Comparative studies of lentivirus infections in other species show that AIDS is not an inevitable outcome of ***i****nfection* ***because simian immunodeficiency virus in natural hosts seldom causes disease****.”*

- Dunham et al., “*The AIDS resistance of naturally SIV-infected sooty mangabeys is independent of cellular immunity to the virus*.”, Blood. **2006** Jul 1;108(1):209-17. Epub 2006 Mar 7, https://www.ncbi.nlm.nih.gov/pubmed/16522814

“These findings indicate that the ***absence of AIDS in naturally SIV-infected sooty mangabeys*** *is independent of a strong cellular immune response to the virus.”*

- HIV-Infektion/AIDS - RKI-Ratgeber, Stand: 08.03.**2016**, https://www.rki.de/DE/Content/Infekt/EpidBull/Merkblaetter/Ratgeber_HIV_AIDS.html

„Reservoir

Einziges bekanntes Reservoir für HIV-1 und HIV-2 ist der Mensch. Schimpansen können mit HIV-1 infiziert werden, ***erkranken aber entweder gar nicht oder erst nach sehr langen Inkubationszeiten***.“

Translation

„The only known reservoir for HIV-1 and HIV-2 is humans. Chimpanzees can become infected with HIV-1, but they either do not get ill at all or only after a very long incubation period.“

Very long incubation time is here to be read as in the order of the life expectancy of healthy animals

Only with especially genetically modified viruses "*AIDS-like*" symptoms can be produced in some monkeys. This does not work for chimpanzees, which is most closely related to man. But, with the missing animal model also the fulfillment of Koch's postulates fails for the HI virus.

Or, conversely, one may ask: if there is this "*deadly disease*" in monkeys, then it has existed for several 10,000 years and not just since 1930 (see above, Worobey et al., **2010**). How did the monkeys survive this? And what about the ancestors of today's humans who consumed these monkeys back then?

In the meantime an explanation is offered on the molecular level why apes still don't get AIDS, cf.

- Warren et al., "*A glycan shield on chimpanzee CD4 protects against infection by primate lentiviruses (HIV/SIV)*.", Proc Natl Acad Sci U S A. **2019** Jun 4;116(23):11460-11469, https://www.ncbi.nlm.nih.gov/pubmed/31113887

and

- Bibollet-Ruche et al., "*CD4 receptor diversity in chimpanzees protects against SIV infection*.", Proc Natl Acad Sci U S A. **2019** Feb 19;116(8):3229-3238, https://www.ncbi.nlm.nih.gov/pubmed/30718403

Beatrice Hahn (co-author in *Bibollet-Ruche et al*.) has been *the* reference for the last 20 years on the putative AID Syndrome in apes and the zoonosis of SIV, i.e. the jump from apes (SI virus) to humans (HI virus).

Both studies, based on local changes in the molecular structure of cell receptors, argue that CD4 cells of the immune system of chimpanzees are protected against infection by the SIV virus (HIV equivalent in apes).

The line of thought is as follows: since apes cannot get AIDS, there must be no infection. However, since there is SIV in apes, the CD4 cells to be destroyed in AIDS must inevitably be protected from infection with the putative trigger, SIV. Something else is not possible according to the virus hypothesis of AIDS. It remains open how the SIV virus multiplies when it cannot enter the cells.

One central assumption is almost lost in both works. Both studies suggest that this protection against the putative HIV virus is absent in humans, as the zoonoses were only 80-100 years ago and man did not have time to adapt genetically to the putative threat.

This is a very far-reaching assumption, the *zoonosis hypothesis of HIV*, for which there is no evidence, see above. But as long as one speculates within the framework of the *scientific consensus*, everything is permissible, cf. above Hahn *et al.* (2000).

The current zoonosis theory lacks every evidence and the missing animal model contradicts Koch's postulates.

Ten years ago *Hahn and co-workers* sounded differently, cf.

- Keele et al., "*Increased mortality and AIDS-like immunopathology in wild chimpanzees infected with SIVcpz*.", Nature. **2009** Jul 23;460(7254):515-9, https://www.ncbi.nlm.nih.gov/pubmed/19626114

Keele et al. (2009) is the essential work to prove that apes can get AIDS. At that time *Keele et al*. postulated a deadly epidemic in apes from ***7 chimpanzees which died or disappeared in 9 years***, cf. ibid,

"For this analysis, only Kasekela and Mitumba chimpanzees of known SIVcpz infection status were included. During the 9-year observation period, ***7 of 17 infected and 11 of 77 uninfected chimpanzees died or disappeared****."*

It was implied that *AIDS-like symptoms* had occurred, among other things based on an analysis of the CD4 cell count. This biomarker is highly error prone, as almost all classical infections in primates lead to a reduction of the CD4 cell count, including sunburn and the *AIDS-defining* tuberculosis, cf. below.

However, everything that is claimed in the sense of the current *consensus theory* is postulated as correct and may be published. This way it becomes science.

With evidence of one ***(1)*** ape in captivity becoming ill ***20 years after the infection***, *Hahn and coworkers* continue to keep the zoonosis hypothesis of a *slow virus* artificially alive, cf.

- Barbian et al., "*Effective treatment of SIVcpz-induced immunodeficiency in a captive western chimpanzee.*", Retrovirology. **2017** Jun 2;14(1):35, https://www.ncbi.nlm.nih.gov/pubmed/28576126

"Here, we report progressive immunodeficiency and clinical disease in ***a*** *captive western chimpanzee (P. t. verus)* ***infected twenty years ago*** *by intrarectal inoculation with an SIVcpz strain (ANT) from a wild-caught eastern chimpanzee (P. t. schweinfurthii)."*

That seems desperate. And it is, for a good reason.

According to ***WHO*** and ***UNAIDS***, every (!) HIV+ measured human should be treated as quickly and intensively as possible with the most severe cytotoxins ("*hit hard and early*"). The serious side effects of the antiretroviral therapy (*ART*) match **1:1** the so-called *HIV related diseases*, in contrast to opportunistic infections, which should occur after **10+ years** as AID Syndrome (*slow virus*), cf. above.

Only when one has found enough distance to ***differentiate between HIV and AIDS again***, one is able to ask the right questions. These questions have been around for a long time, but the discussion is lacking, cf.

- Marx et al., "*AIDS as a zoonosis? Confusion over the origin of the virus and the origin of the epidemics*.", J Med Primatol. **2004** Oct;33(5-6):220-6, https://www.ncbi.nlm.nih.gov/pubmed/15525322

"Based on findings demonstrating the simian ancestry of HIV, AIDS has been reported to be a zoonosis. ***However, this theory has never been proved and must seriously be questioned****. Several arguments show that HIV-AIDS is not a zoonosis."*

"*If AIDS were a simple zoonosis with potential to become a health threat in humans as reported [31], it would have appeared earlier in Africa and would have emerged in the West during the era of slave trade when millions of Africans were brought to North and South America [33]."*

Even if there is a HI virus, it is very doubtful that it causes AIDS in humans, when at the same time the homolog in monkeys (SIV), which is said to be the precursor, does not cause AIDS in monkeys.

Why is this important?

AIDS has only existed since the early 1980s. The first 5 cases were reported in 1981, cf.

- Gottlieb et al., "*Pneumocystis Pneumonia - Los Angeles*", Morbidity and mortality weekly report, Vol. 30, no. 21, June 5, **1981**, https://stacks.cdc.gov/view/cdc/1261

So the cause of AIDS can only exist since that time.

A virus that has been in contact with humans for thousands of years, be it the SIV virus in monkeys or the putative HI virus without causing this disease, it is out of the question as a pathogen. Because then AIDS would have existed for millennia.

Ibid, Marx et al., "*There is no evidence that a person can contract AIDS from a monkey or chimpanzee. There is still a missing link.*"

Apes do not use drugs.

9. The '*molecular clock*' problem

We have to go back once more to Worobey *at al.* (2010) and the age of SIV of 32.000+ years determined from phylogenetic analysis. In this context there is another problem with the theory that is little known outside the specialist circles.

To do this, one has to envision the reasoning why HIV supposedly is pathogenic (= makes you sick) and SIV is not pathogenic (= does not make you sick): after the alleged ***7x*** (or even ***13x***) zoonoses around *1930*, see above, there was not enough time for humans to adapt to this new *threat*. It is the same argument that science uses in many supposed *zoonosis threat scenarios*. For this to work it is important that HIV in the phylogenetic analysis is very young and SIV rather old.

At first it seems to look quite like that, at least if we look at the phylogenetic analysis of HIV, cf.

- Korber et al., "*Timing the ancestor of the HIV-1 pandemic strains*.", Science. **2000** Jun 9;288(5472):1789-96, https://www.ncbi.nlm.nih.gov/pubmed/10846155

"Using a comprehensive full-length envelope sequence alignment, we estimated the date of the last common ancestor of the main group of HIV-1 to be ***1931*** *(1915-41). Analysis of a gag gene alignment, subregions of envelope including additional sequences, and a method that relaxed the assumption of a strict* ***molecular clock*** *also supported these results"*

On the procedure and the determination of the '*molecular clocks'* as well as the related problems cf. also

- Holmes, "*Molecular Clocks and the Puzzle of RNA Virus Origins*", J Virol. **2003** Apr; 77(7): 3893–3897, https://www.ncbi.nlm.nih.gov/pubmed/12634349

*„**The key to establishing a timescale of viral evolution lies in accurately determining the rate of nucleotide substitution.** Most analyses undertaken to date suggest that the average rate of nucleotide substitution in RNA viruses is ~10^{-3} substitutions per site per year, with an approximately fivefold range around this (21). The fact that broadly similar rates are found in RNA viruses with very different genome organizations and lifestyles implies that both the error rate associated with RNA polymerase, estimated to be about one mutation per genome replication (10), and the rate of viral replication are roughly constant. If the average substitution rate of ~10^{-3} substitutions/site/year is accurate, then, on average, every nucleotide position will have fixed 1 substitution after ~1,000 years of evolution (corresponding to an average divergence time between two lineages of only 500 years)."*

"However, in some cases such a recent origin conflicts with other evolutionary data. ***Perhaps the most notorious example is that of the primate lentiviruses, which include the human immunodeficiency virus types 1 and 2 (HIV-1 and HIV-2) and a growing list of simian immunodeficiency viruses (SIVs) that infect a wide variety of African monkeys (19).*** *At face value, it would appear that these viruses have been associated with their host species for millions of years.* ***Not only are they asymptomatic in their natural hosts****, which when compared to the high virulence of HIV suggests that they have evolved stable associations over an extended time period, but the phylogenies of the viruses and the hosts often match, which implies that the viruses and the hosts have undergone cospeciation. Although the divergence times of the primate species in*

question are often uncertain, ***it is clear that virus-host cospeciation must mean a viral evolutionary history dating back millions of years****."*

The very wide distribution of SIV in over 40 species of monkeys, as well as the presence of similar lentiviruses in rabbits, cats, sheep, cattle, etc., suggests that these lentiviruses have existed for a very long time, millions of years. The fact that they cause no symptoms in these hosts also suggests that the host and the virus have been coexisting for a long time.

The extremely high mutation rate of HIV results in a very short phylogenetic age. However, the same conclusion also applies to the closely related SI virus and all other lentiviruses, which also have a very high mutation rate as RNA viruses. Evaluating by the same principles the *'molecular clocks '* of SI viruses as Korber *et al.* (2000) did for the HI virus, we get the astonishing result that SIVcpz is approx. ***500 years*** old and SIVsmm approx. ***200 years***, cf.

- Wertheim, Worobey, "*Dating the age of the SIV lineages that gave rise to HIV-1 and HIV-2*.", PLoS Comput Biol. **2009** May;5(5):e1000377, https://www.ncbi.nlm.nih.gov/pubmed/19412344

"Here, we use relaxed molecular clock dating techniques to estimate the time of most recent common ancestor for the SIVs infecting chimpanzees and sooty mangabeys, the reservoirs of HIV-1 and HIV-2, respectively. The date of the most recent common ancestor of SIV in chimpanzees is estimated to be ***1492*** *(1266-1685), and the date in sooty mangabeys is estimated to be* ***1809*** *(1729-1875)."*

"Comparisons between the SIV most recent common ancestor dates and those of the HIV lineages suggest a ***difference on the order of only hundreds of years****. Our results suggest either that SIV is a surprisingly young lentiviral lineage or that SIV and, perhaps, HIV dating estimates are seriously compromised by unaccounted-for biases."*

Obviously, that doesn't go together. However, there is no reason why *'molecular clocks'* in chimpanzees should differ from those in humans. The genetic relationship seems too close for this.

The methods for the identification of RNA fragments have only been around since the 1960s. And new methods were introduced only on a large scale together with the alleged HIV (*not AIDS*!) epidemic starting in the 1990s. Lack of the technical possibility, there is simply no data before this period.

One should not assume an age of the HIV groups of approximately 80 - 100 years without considering the consequences of the same considerations for all other lentiviruses, including SIV, and the resulting age of 500 and 200 years respectively. However, that is exactly what is happening.

If the very wide distribution and the high number of SI virus groups speak for a high phylogenetic age, then the question arises why the same should not also apply to the HI virus groups. This is another contradiction in the virus theory of AIDS, which is still waiting for an explanation due to the lack of discussion.

In fact, it seems that zoonoses are not as common and, above all, not as inevitable, as Hahn, Keele, Korber, Worobey & Co. assume without further proof, cf.

- Leendertz et al., "*No evidence for transmission of SIVwrc from western red colobus monkeys (Piliocolobus badius badius) to wild West African chimpanzees (Pan troglodytes verus) despite high exposure through hunting*.", BMC Microbiol. **2011** Feb 1;11(1):24, https://www.ncbi.nlm.nih.gov/pubmed/21284842

10. AIDS vaccination

The chapter on a vaccine against AIDS, or according to the prevailing opinion against the HI virus, can be kept short.

The principle of vaccination involves the provocation of the production of antibodies against the pathogen by attenuated pathogens or fragments of pathogens, as well as the production of memory cells. This is not necessary for HIV+ measured people. They already carry these antibodies in themselves. More specific, they were declared HIV+ because of these antibodies.

As shown below ("*bystander cell enigma*"), HIV+ measured people are not immunosuppressed. CD4 cells are generated in large numbers every day.

Here, it is completely unclear what an HIV / AIDS vaccine should do better than the human body already does today.

The HI virus is the only virus in which immunization by antibodies supposedly does not work. That is very questionable. Viruses are neutralized *in vivo* within a few days to a few weeks by antibodies. Damage caused by a virus occurs in this phase, the acute phase. But not years later (the putative *slow virus* concept).

The consequences of a flu infection are felt within the acute phase, i.e. within about 4 weeks. But not 10 years after the flu. And even assuming such consequences, they would not occur in 100% of all cases, i.e. in every single case.

11. Diagnosis: cross reactions and manufacturer's statements

An analysis of the cross-reactions of HIV Ag / Ab tests, and in particular HIV rapid tests (RDT) reveals a staggering number of cross-reactions. That means that the tests respond to proteins in the human body, e.g. in the blood, which have nothing to do with a suspected HI virus.

11.1. Cross reactions of HIV Ag / Ab tests

Below cross reactions are shown by their cause. Particularly affected are pregnant women. This is probably not by chance, as the placenta shows increased retroviral activity even without any HI virus, see HERV below.

There are also other cross reactions, e.g. after flu vaccinations or co-infections, such as, **herpes**, **hepatitis A**, **hepatitis B**, **malaria**, **parasites**, **rheumatoid factor** or **tuberculosis**. In particular, cross-reactions to malaria, tuberculosis or parasites are of particular importance in developing countries.

Pregnancy

The fact that pregnant women in particular often cross react to HIV Ag / Ab tests may have systematic causes. As shown below, the placenta shows natural retroviral activity. HIV+ women are very rare (see below, transmission rates in heterosexual couples). Due to the rarity (very low prevalence), the positive predictive value (PPV) of HIV self-tests in women is <1%, see also, Annex I.

- Akl et al. *"A case of false-positive test results in a pregnant woman of unknown HIV status at delivery."*, Lab Med. **2014** Summer;45(3):259-63, https://www.ncbi.nlm.nih.gov/pubmed/25051080

- Simoncini et al. "*Reducing False Positive HIV Diagnosis in Niger: A Women's issue*",J. Int. Assoc. Prov. AIDS C., **2016** Vol. 15(1) 15–18, http://journals.sagepub.com/doi/pdf/10.1177/2325957415586260

- Hsiao N-Y et al. "*Misdiagnosed HIV infection in pregnant women initiating universal ART in South Africa*", J. Int. AIDS Soc. **2017**, 20(Suppl 6):21758, http://journals.sfu.ca/jias/index.php/jias/article/viewFile/21758/pdf

- Doran et al. "*False-positive and indeterminate human immunodeficiency virus test results in pregnant women*.", Arch Fam Med. **2000** Sep-Oct;9(9):924-9, https://www.ncbi.nlm.nih.gov/pubmed/11031402

"False-positive ELISA test results can be caused by alloantibodies resulting from transfusions, transplantation, or pregnancy, autoimmune disorders, malignancies, alcoholic liver disease, or for reasons that are unclear."

*"**The WB is not used as a screening tool because…it yields an unacceptably high percentage of indeterminate results (10%-49%).**"*

- Zacharias et al. „*High false-positive rate of human immunodeficiency virus rapid serum screening in a predominantly hispanic prenatal population.*", J Perinatol. **2004** Dec;24(12):743-7, https://www.ncbi.nlm.nih.gov/pubmed/15318249

- Chao et al. "*Risk Factors Associated with False Positive HIV Test Results in a Low-Risk Urban Obstetric Population*", J Pregnancy., **2012**: 841979, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3155785/

- Shima-Sano et al., "*A human immunodeficiency virus screening algorithm to address the high rate of false-positive results in pregnant women in Japan*.", PLoS One. **2010** Feb 23;5(2):e9382, https://www.ncbi.nlm.nih.gov/pubmed/20186348

- Yarbrough, Anderson, "*The Brief Case: A Reactive HIV Rapid Antibody Test in a Pregnant Woman*", J Clin Microbiol. **2016** Apr; 54(4): 826–828, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4809934/

*"Though her antigen/antibody test was also positive, the negative HIV-1/2 differentiation assay and negative molecular test ruled out a diagnosis of HIV. **Her initial rapid antibody and antigen/antibody screening tests were therefore false positives**."*

- Adhikari et al., "*Diagnostic accuracy of fourth-generation ARCHITECT HIV Ag/Ab Combo assay and utility of signal-to-cutoff ratio to predict false-positive HIV tests in pregnancy*.", Am J Obstet Gynecol. **2018** Oct; 219(4):408.e1-408.e9, https://www.ncbi.nlm.nih.gov/pubmed/29913173

*„Of these, 33 of 190 (17%) women had false-positive HIV screening tests, …***"**

And here the transfer of the diagnosis to PCR, which is not permitted according to the manufacturers, see below:

"*When the qualitative RNA assay result is unavailable, absence of risk factors in combination with an ARCHITECT HIV Ag/Ab assay S/Co ratio <5 and nonreactive differentiation assay provide sufficient evidence to support **deferral of unnecessary intrapartum interventions while awaiting qualitative RNA results.**"*

- Jenn Morson, „*How I Tested HIV Positive — Nine Times — While Pregnant*", May 25 **2016**, https://www.ozy.com/true-story/how-i-tested-hiv-positive-nine-times-while-pregnant/68859

9x false positive test results during pregnancy. Should we not we start investigating if there is no systematic cause for false positives in pregnant women?

Classical infections and cancer

- Liu et al. *„Spectrum of false positivity for the fourth generation human immunodeficiency virus diagnostic tests",* AIDS Res Ther. **2016**; 13: 1, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4700595/

Positive rheumatoid factor, toxoplasmosis, herpes simplex, antibodies against mouse proteins

- Package insert Alere Determine HIV–1/2 Ag/Ab Combo, p. 4 No. 12,
(Limitations of the test)
https://www.fda.gov/downloads/biologicsbloodvaccines/bloodbloodproducts/approvedproducts/premarketapprovalspmas/ucm364698.pdf

*„Specimens from individuals with **Toxoplasma IgG**, **human anti-mouse antibodies**, **rheumatoid factor**, elevated triglycerides (above 600 mg/dL), **herpes simplex virus infection**, and hospitalized and cancer patients may give false positive test results.“*

- Li et al., "*False human immunodeficiency virus test results associated with rheumatoid factors in rheumatoid arthritis*.", Chin Med Sci J. **2014** Jun;29(2):103-6,
https://www.ncbi.nlm.nih.gov/pubmed/24998232

Alcohol abuse

- Novick, "*Specificity of antibody tests for human immunodeficiency virus in alcohol and parenteral drug abusers with chronic liver disease*.", Alcohol Clin Exp Res. **1988** Oct;12(5):687-90,,
https://www.ncbi.nlm.nih.gov/pubmed/3067617

*„Compared to true-negatives, **false-positives had significantly more years of alcohol abuse**, younger ages of onset of alcohol abuse, greater frequencies of jaundice and edema, higher levels of alkaline phosphatase, total billirubin, total protein, and globulins, and lower levels of serum albumin. In a stepwise logistic regression, only hyperglobulinemia was significantly associated with a false-positive anti-HIV*."

Alcohol abuse is very common in risk groups.

Cytomegalo virus

- Bronze et al., "*False-positive enzyme immunoassay for HIV due to acute cytomegalovirus infection*", Clinical Infectious Diseases, 27 (**1998**) 221-2, https://www.ncbi.nlm.nih.gov/pubmed/9675487

Hepatitis A

- Huffmann et al. „*Report of a False Positive Rapid HIV test due to Hepatitis A in a U.S. Army Soldier*", Clin Res HIV AIDS Pre, **2014**, Issue No: 2324-7339,
https://www.researchgate.net/publication/286419120_Report_Of_A_False_Positive_Rapid_HIV_Test_Due_To_Hepatitis_A_In_A_US_Army_Soldier

Hepatitis B vaccination

- Lee et al. *"HIV false positivity after hepatitis B vaccination",* Lancet. **1992** Apr 25;339(8800):1060, https://www.ncbi.nlm.nih.gov/pubmed/1349089

Hepatitis B

- Wai, Tambyah, "*False-positive HIV-1 ELISA in patients with hepatitis B*", American Journal of Medicine, 112 (**2002**) 737, https://www.amjmed.com/article/S0002-9343(02)01113-0/fulltext

(see also below, Annex III: *„Bis zu 95 % aller HIV-infizierten Patienten haben eine Hepatitis B durchgemacht, etwa 10–15 % haben eine chronische Hepatitis B."*

Translation:

„Up to 95% of all HIV-infected patients have undergone hepatitis B, about 10-15% have chronic hepatitis B.")

- Isaacman, "*Positive HIV antibody test results after treatment with hepatitis B immune globulin*.", JAMA. **1989** Jul 14;262(2):209, https://www.ncbi.nlm.nih.gov/pubmed/2739013

Rubella vaccination

- Araujo et al., "*Rubella vaccination and transitory false-positive test results for HIV Type 1 in blood donors*", Transfusion, 49 (**2009**) 2516-17, https://www.ncbi.nlm.nih.gov/pubmed/19788507

Tetanus vaccination

- Gonnelli et al., "*Transiently positive HIV antibody test after treatment with tetanus immune globulin.*", Lancet. **1991** Mar 23;337(8743):731, https://www.ncbi.nlm.nih.gov/pubmed/1672192

Leprosy

- Hussain et al. *„Serum samples from patients with mycobacterial infections cross-react with HIV structural proteins Gp41, p55 and p18* ", Lepr Rev (**2007**) 78, 137 – 147, https://www.lepra.org.uk/platforms/lepra/files/lr/June07/Lep137-147.pdf

- Andrade et al., "*Leprosy as a cause of false-positive results in serological assays for the detection of antibodies to HIV-1*", International Journal of Leprosy, 59 (**1991**) 125, https://www.ncbi.nlm.nih.gov/pubmed/2030312

- Kashala et al. *„Infection with human immunodeficiency virus type 1 (HIV-1) and human T cell lymphotropic viruses among leprosy patients and contacts: correlation between HIV-1 cross-reactivity and antibodies to lipoarabinomannan.",* J Infect Dis. **1994** Feb;169(2):296-304, https://www.ncbi.nlm.nih.gov/pubmed/7906291

"***Sera from leprosy patients and leprosy contacts were often false-positive for HIV-1 by ELISA and were indeterminate by Western blot***. *LAM IgM and PGL-I IgM antibodies in sera from leprosy patients* ***yielded significant cross-reactivities with HIV-1 pol and gag proteins***."

"*Caution should be exercised when interpreting HIV-1 ELISA and Western blot data from regions where leprosy or other mycobacterial diseases are endemic.*"

Cf. below, *AIDS and Africa*.

Flu vaccination

- Erickson et al. „*Influenza Vaccination and False Positive HIV Results* ", N Engl J Med **2006**; 354:1422-1423, https://www.nejm.org/doi/full/10.1056/NEJMc053417

- Mac Kenzie et al., "*Multiple false-positive serologic tests for HIV, HTLV-1 and hepatitis C following influenza vaccination*, 1991" JAMA, 268 (**1991**) 1015-7, https://www.ncbi.nlm.nih.gov/pubmed/1501307

- Challakere & Rapaport , "*False-positive HIV type 1 ELISA results in low-risk subjects*", Western Journal of Medicine, 159 (**1993**) 214-5, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1022242/

- Arnold et al. "*Donor follow-up of influenza vaccine-related multiple viral enzyme immunoassay reactivity*.", Vox Sang. **1994**;67(2):191-4, https://www.ncbi.nlm.nih.gov/pubmed/7801610

Malaria

- Fonseca et al. „*Cross-reactivity of anti-Plasmodium falciparum antibodies and HIV tests*", Trans R Soc Trop Med Hyg. **2000** Mar-Apr;94(2):171-2, https://www.ncbi.nlm.nih.gov/pubmed/10897359

- Gasasira et al. „*False-Positive Results of Enzyme Immunoassays for Human Immunodeficiency Virus in Patients with Uncomplicated Malaria*", J Clin Microbiol. **2006** Aug; 44(8): 3021–3024, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1594619/

- Ohanu et al. "*Can Malaria Interfere with the Diagnosis of HIV Infection?*", Int J Trop Dis & Health 18(1): 1-4, **2016**, https://www.researchgate.net/publication/305458422_Can_Malaria_Interfere_with_the_Diagnosis_of_HIV_Infection

- Stempel et al., "*False positive fourth generation HIV test in a patient with severe malaria.",* Int J Infect Dis. **2019** Jun; 83:86-87, Epub 2019 Apr 13, https://www.ncbi.nlm.nih.gov/pubmed/30986542

*"**False positive HIV results have been reported in a myriad of different settings**—schistosomiasis, systemic lupus erythematosus, influenza vaccination (Erickson et al., 2006, Gasasira et al., 2006, Everett et al., 2010)—leading to significant patient distress and mistrust of providers. Although the majority of false positive testing has been reported with earlier generation assays and rapid diagnostic tests, **false positive 4th generation assays have been reported** (Klarkowski et al., 2014, Liu et al., 2016). Anti-P. falciparum antibody cross reactivity with HIV-1/-2 antibodies on second and third generation assays is well documented*

(Fonseca et al., 2000, Gasasira et al., 2006). To our knowledge, this is the first case of a false positive 4th generation HIV assay due to severe acute malaria."

That happened in the USA. What would happen in Africa, India or Pakistan where most malaria infected persons live?

Parasites

- Everett et al. „*Association of Schistosomiasis with False-Positive HIV Test Results in an African Adolescent Population* ", J. Clin. Microbiol. May **2010** vol. 48 no. 5 1570-1577, http://jcm.asm.org/content/48/5/1570.full

- Lejon et al. „*Low Specificities of HIV Diagnostic Tests Caused by Trypanosoma brucei gambiense Sleeping Sickness*", J. Clin. Microbiol. August **2010** vol. 48 no. 8 2836-2839, http://jcm.asm.org/content/48/8/2836

- Shanks et al., "*Accounting for False Positive HIV Tests: Is Visceral Leishmaniasis Responsible?"*, PLoS One. **2015** Jul 10;10(7):e0132422, http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0132422

- Parra-Pineros et al., "*False-positive HIV test and Trypanosoma cruzi infection in eastern Colombia*", Southern Medical Journal,97 (**2004**) 423-4, https://www.ncbi.nlm.nih.gov/pubmed/15108844

- Salinas et al., "*Patients with leishmaniasis can have false-positive HIV test results*", Clinical Infectious Diseases, 45 (**2007**) 139-140, https://academic.oup.com/cid/article/45/1/139/480097

- Smotrys, et al., "*Babesiosis as a cause of false-positive HIV serology*.", BMJ Case Rep. 2018 Jun 8; **2018**, https://www.ncbi.nlm.nih.gov/pubmed/29884713

- Mesiha et al., "*False Positive HIV Result and Low CD4 in Babesiosis*.", Ann Clin Lab Sci. **2017** Aug;47(4):516-517, https://www.ncbi.nlm.nih.gov/pubmed/28801382

Tuberkulosis

- Swaminathan et al. „*Prevalence and pattern of cross-reacting antibodies to HIV in patients with tuberculosis*", AIDS Res Hum Retroviruses. **2008** Jul;24(7):941-6, https://www.ncbi.nlm.nih.gov/pubmed/18593340

- De Cock et al. „*Cross-reactivity on western blots in HIV-1 and HIV-2 infections*", AIDS. **1991** Jul;5(7):859-63, https://www.ncbi.nlm.nih.gov/pubmed/1892591

Placental tissue

A cross-reaction with normal placental tissue in HIV tests for HIV antibodies is extremely critical as all people are supplied with blood and nutrients via the placenta during the first 9 months of life. It is not entirely clear why this circumstance is given no greater attention because it correlates with the frequent cross-reactions in

pregnant women.

- Lyden et al. *„Anti-HIV monoclonal antibodies cross-react with **normal** human tropoblast*“, Trophoblast Research 8:19-32, **1994,** https://www.placentajournal.org/article/S0143-4004%2805%2980333-9/pdf

- Lyden et al., “*Expression of endogenous HIV-1 cross-reactive antigens within normal human extravillous trophoblast cells*”, Journal of Reproductive Immunology, 28 (**1995**) 233-45, https://www.ncbi.nlm.nih.gov/pubmed/7473433

- Faulk et al. *„HIV proteins in **normal** human placentae*“, Am J Reprod Immunol. **1991** Apr;25(3):99-104, https://www.ncbi.nlm.nih.gov/pubmed/1930645

Heterophilic anti bodies

- Spencer et al., “*Heterophilic antibody interference causing false-positive rapid human immunodeficiency virus antibody testing*.”, Clin Chim Acta. **2009** Jan;399(1-2):121-2, https://www.ncbi.nlm.nih.gov/pubmed/18950610

- Willman et al., “*Heterophile antibodies to bovine and caprine proteins causing false-positive human immunodeficiency virus type 1 and other enzyme-linked immunosorbent assay results.*”, Clin Diagn Lab Immunol. **1999** Jul;6(4):615-6, https://www.ncbi.nlm.nih.gov/pubmed/10391873

Dialysis patients

- Silverstein et al., “*False-positive HIV antibody test in a dialysis patient*”, Pediatric Nephrology, 19 (**2004**) 547-9, https://www.ncbi.nlm.nih.gov/pubmed/14991392

Pre-exposure prophylaxis (PrEP)

As already mentioned above, there are increasing efforts in the risk group area (MSM) to use prophylaxis to prevent a supposed infection. This is called PrEP and it does not protect against false positives.

- Stekler et al., “*Repeated False-Positive HIV Test Results in a Patient Taking HIV Pre-Exposure Prophylaxis*.”, Open Forum Infect Dis. **2018** Sep 26;5(9), https://www.ncbi.nlm.nih.gov/pubmed/30276221

- Ndase et al., “*Frequency of false positive rapid HIV serologic tests in African men and women receiving PrEP for HIV prevention: implications for programmatic roll-out of biomedical interventions.*”, PLoS One. **2015** Apr 17;10(4), https://www.ncbi.nlm.nih.gov/pubmed/25885664

“*In the active PrEP arms, **over two-thirds of visits with positive rapid test results were false positive results** (69.2%, 110 of 159), …”*

Other False Positives

- Sayre et al., "*False-positive human immunodeficiency virus type 1 western blot tests in noninfected blood donors*", Transfusion Vol 36 (1), Jan **1996**, p. 45-52, https://onlinelibrary.wiley.com/doi/pdf/10.1046/j.1537-2995.1996.36196190514.x

- Nastouli et al., "*False-positive HIV antibody results with ultrasensitive serological assays in uninfected infants born to mothers with HIV.",* AIDS. **2007** May 31;21(9):1222-3, https://www.ncbi.nlm.nih.gov/pubmed/17502739

"*Using this assay in 18 infants with three consecutive negative HIV-DNA PCR we found that eight were antibody negative (age range18–24 months), and 10 were positive (age range 19–20 months).* ***Of the 10 infants positive by the fourth-generation assay, nine were negative by our previous third-generation HIV assay (performed simultaneously). Repeat fourth-generation EIA testing was negative for nine infants within a few months, confirming waning levels of maternal antibody and not emerging infection***."

- Jindal et al., "*False positive tests for HIV in a woman with lupus and renal failure*", New England Journal of Medicine, 328 (**1993**) 1281-2, https://www.nejm.org/doi/full/10.1056/NEJM199304293281717

- Mylonakis et al., "*Report of a false-positive HIV test result and the potential use of additional tests in establishing HIV serostatus*.", Arch Intern Med. **2000**, Aug 14-28;160(15):2386-8, https://www.ncbi.nlm.nih.gov/pubmed/10927739

- Seme et al., "*False-positive result of a confirmatory HIV line immuno assay in an apparently healthy individual — a case report*", Collegium Antropologicum, 30 (suppl. 2, **2006**) 43-6, https://www.ncbi.nlm.nih.gov/pubmed/17508473

- Baveewo et al., "*Potential for false positive HIV test results with the serial rapid HIV testing algorithm*", BMC Res Notes. **2012** Mar 19;5:154, https://www.ncbi.nlm.nih.gov/pubmed/22429706

"*Of the 3388 individuals who were tested, 984 were HIV positive on two consecutive tests, and 29 were considered positive by a tiebreaker (positive on Determine, negative on STAT-PAK, and positive on Uni-Gold).* ***However, when the 29 samples were further tested using qualitative DNA PCR, 14 (48.2%) were HIV negative."***

Which test is decisive? As shown below, manufacturers reject PCR as a diagnostic tool. What is expected of the patient here?

- Willman et al. "*Heterophile antibodies to bovine and caprine proteins causing false-positive human immunodeficiency virus type 1 and other enzyme-linked immunosorbent assay results*.", Clin Diagn Lab Immunol. **1999** Jul;6(4):615-6, https://www.ncbi.nlm.nih.gov/pubmed/10391873

"*We describe here a 22-month-old child with heterophile antibodies reactive with bovine serum albumin and caprine proteins* ***causing false-positive results to human immunodeficiency virus type 1*** *and other infectious serology testing*"

- Sheikh et al. “High frequency of false positive results in HIV screening in blood banks.”, J Ayub Med Coll Abbottabad. **2004** Jan-Mar;16(1):28-31, https://www.ncbi.nlm.nih.gov/pubmed/15125176

“*Out of 5000 subjects, 48 (0.96%) were positive for HIV-1/2 on Strategy I,* ***37 (77% of 48) met the criteria of false positive,*** *while only 11 (0.22% of 5000) were found to be true positive.”*

- Wood et al., “*Two "HIV-infected" persons not really infected*.”, Arch Intern Med. **2003** Aug 11-25;163(15):1857-9, https://www.ncbi.nlm.nih.gov/pubmed/12912724

- Shida et al., “*False-positive human immunodeficiency virus antibody test and autoimmune hemolytic anemia in a patient with angioimmunoblastic T-cell lymphoma*.”, Intern Med. **2011**;50(20):2383-7, https://www.ncbi.nlm.nih.gov/pubmed/22001471

- Dirweesh et al., “*False Positive Human Immunodeficiency Virus Antibody Test in a Patient with Mediastinal Hodgkin Lymphoma*”, ATS Conference **2017**, C80-I. THORACIC ONCOLOGY CASE REPORTS III, https://www.atsjournals.org/doi/abs/10.1164/ajrccm-conference.2017.195.1_MeetingAbstracts.A6676

- Esteva, “*False positive results for antibody to HIV in two men with systemic lupus erythemat*osus.”, Ann Rheum Dis. **1992** Sep;51(9):1071-3, https://www.ncbi.nlm.nih.gov/pubmed/1417140

- Lang *et al*., “*HIV misdiagnosis: A root cause analysis leading to improvements in HIV diagnosis and patient care*", J. Clin. Viro. 96 (**2017**), 84 - 88, https://www.ncbi.nlm.nih.gov/pubmed/29031156

“Technical and human factors were identified as being causative in this HIV misdiagnosis including (i) ***high rates of false reactive results on the Abbott ARCHITECT HIV-1&2 COMBO EIA****,…”*

“CONCLUSIONS: HIV testing remains problematic despite significant advances in HIV test performance and algorithm development, presenting new and unexpected issues.”

As of **2017**.

It is very doubtful that this amount of documented false positives is solely cause by handling errors.

- Coleman, “*False-positive HIV diagnoses: lessons from Ugandan and Russian research cohorts*.”, HIV Clin Trials. **2018** Feb;19(1):15-22, https://www.ncbi.nlm.nih.gov/pubmed/29384717

“*In both Russia & Uganda, undetectable viremia was much higher than would be expected for an HIV-infected ART-naïve cohort. Misclassification of study participants was due to misdiagnosis of HIV with rapid diagnostic testing and inaccurate accounting of ART use*.”

As of **2018**.

- Kosack et al., "*Towards more accurate HIV testing in sub-Saharan Africa: a multi-site evaluation of HIV RDTs and risk factors for false positives*.", J Int AIDS Soc. **2017** Mar 24;19(1):21345, https://www.ncbi.nlm.nih.gov/pubmed/28364560

*"., **individual RDTs performed more poorly than in the WHO evaluations: only one test met the recommended thresholds for RDTs of ≥99% sensitivity and ≥98% specificity**. By performing all tests in a centralized setting, we show that these differences in performance **cannot be attributed to study procedure, end-user variation, storage conditions, or other methodological factors**. These results highlight the **existence of geographical and population differences in individual HIV RDT performance** and underscore the challenges of designing locally validated algorithms that meet the latest WHO-recommended thresholds."*

"*Towards more accurate HIV testing*": isn't that 30 years too late? Only 1 test met the WHO requirements for sensitivity and specificity. As shown in Annex I, these WHO guidelines are not sufficient. Due to the low prevalence of HIV, there the positive predictive value (PPV) results to <1% for non-risk groups.

HERV and HIV

In human cells, residual levels of retroviral activity (HERV) can be detected. The now endogenous viruses are supposed to have found their way into the human genome in the course of evolution. It is assumed that the proportion of the human genome is about 8%. However, extreme caution is required with this value. https://en.wikipedia.org/wiki/Endogenous_retrovirus#Human_endogenous_retroviruses.

This is also due to the fact that the DNA of the mammalian cell is not simply translated linearly, but after transcription the RNA is cut together. Added to this is the fact that genes can change their position in the genome (transposition). That means what information is contained in the genome cannot be simply extrapolated linearly from the base sequence.

In addition, the term HERV is somewhat imprecise, as no one has observed the infection with a retrovirus 1 million years ago. For the moment, it is just pointed out that there is natural reverse transcriptase activity in the human cell, which also leads to cross-reactivity in HIV Ag / Ab tests.

- Haist et al. „ *Reactivities of HIV-1 gag-Derived Peptides with Antibodies of HIV-1-Infected and Uninfected Humans*", AIDS RESEARCH AND HUMAN RETROVIRUSES, Vol 8, No 11, 1909:1917, **(1992)** https://epub.uni-regensburg.de/20412/1/wolf11.pdf

*"**Amino acid sequence comparison of HIV-1 gag proteins with those of human endogenous retroviruses (ERV K10, ERV 3) revealed significant similarities** predominantly in the domains showing elevated antibody cross-reactions."*

"Sera of HIV- humans showed reactivity against four defined regions, two in p17, one in p24, and one in p15."

*„The fact, that HIV- sera show cross-reactivities especially with those protein regions that also show enhanced reactivities in HIV-1+ serum samples implies that similar sequences have already **been exposed to the immune system prior to HIV infection**." (S. 1915)*

- Tandon et al., *„Identification of Human Endogenous Retrovirus-Specific T Cell Responses in Vertically HIV-1-Infected Subjects*"; J. Vir., Nov. **2011** , Vol. 85, No. 21,, p. 11526–11531 https://www.ncbi.nlm.nih.gov/pubmed/21880743

"*HERV (-H, -K, and -L family)-specific T cell responses were identified in 26 of 42 subjects, with the greatest magnitude observed for the responses to HERV-L*."

This already suggests that it may be difficult to distinguish between natural, endogenous retroviral activity and putative infectious, exogenous retroviral activity. More about HERV below.

No security through multiple tests (tie-breaker)

Even the cascading of several tests does not provide security. It is possible that the patient will be tested until the patient agrees to a treatment:

- Shanks et al. "*Evaluation of HIV testing algorithms in Ethiopia: the role of the tie-breaker algorithm and weakly reacting test lines in contributing to a high rate of false positive HIV diagnoses."*, BMC Infect Dis. **2015** Feb 3;15:39, https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-015-0769-3

"*The risk of false positive HIV diagnosis in a tiebreaker algorithm is significant*."

With that amount of cross-reaction, you'd think professional bodies knew about it and have something to say about it. Yes, that's the way it is. Cf.

Gemeinsamen Diagnostikkommission der Deutschen Vereinigung zur Bekämpfung von Viruskrankheiten e. V. (DVV e. V.) und der Gesellschaft für Virologie e. V. (GfV e. V.)

Translation

„Joint Diagnostic Commission of the German Association for the Control of Viral Diseases e. V. (DVV e.V.) and the Society for Virology e. V. (GfV e.V.)"

- Rabenau et al., *„Nachweis einer Infektion mit Humanem Immundefizienzvirus (HIV): Serologisches Screening mit nachfolgender Bestätigungsdiagnostik durch Antikörper-basierte Testsysteme und/oder durch HIV-Nukleinsäure-Nachweis*", Bundesgesundheitsbl **2015** · 58:877–886, http://www.dvv-ev.de/news/HIV-Diagnostik_Bundesgesundheitsblatt_2015.pdf;jsessionid=9953B353E4D1AAB755F015F7F10D0F31.2_cid298.pdf

Translation

"Federal Health Bulletin"

„Detection of Human Immunodeficiency Virus (HIV) Infection: Serological Screening with Subsequent Confirmatory Diagnosis by Antibody-Based Assay Systems and / or by HIV-Nucleic Acid Detection"

p. 881

„Die Verwendung von zwei oder drei unterschiedlichen HIV-Screeningtests für die HIV-Stufendiagnostik wird von der WHO insbesondere für Hochprävalenz-Regionen mit begrenzten Ressourcen empfohlen. Dabei werden entweder generell zwei unterschiedliche Screening-tests (meist immunchromatographische Schnelltests) durchgeführt oder der zweite Screeningtest nur bei reaktivem erstem Test. Übereinstimmend reaktive Ergebnisse werden als Beweis einer HIV-Infek-tion angesehen und diskrepante Ergebnisse entweder mit einem dritten Test (Tie-Breaker) oder über eine Verlaufskontrolle, wie in Abschn. 2.1 beschrieben, abgeklärt."

Translation

„The use of two or three different HIV screening tests for HIV step-by-step diagnosis is recommended by the WHO especially for high-prevalence regions with limited resources. Either generally two different screening tests (usually rapid immunochromatographic tests) are carried out or the second screening test only with a reactive first test. Consistently reactive results are considered to be evidence of HIV infection and discrepant results are assessed by either a third test (Tie-Breaker) or by follow-up as described in Section 2.1."

***„Für Deutschland wird eine solche Strategie wegen der niedrigen HIV-Prävalenz nicht empfohlen**. Insbesondere ist der **positive prädiktive Wert zweier übereinstimmend reaktiver Screeningtests immer noch so niedrig**, dass hier unbedingt eine weitere Bestätigungsdiagnostik, wie oben beschrieben, erfolgen muss. Allerdings ist bei Verwendung von zwei hochempfindlichen Screeningtests der **negative prädiktive Wert bei diskrepanten Testergebnissen sehr hoch**, speziell in Niedrig-Risiko-Kollektiven, wie etwa beim Schwangeren-Screening*."

Translation

*„**For Germany, such a strategy is not recommended because of low HIV prevalence.** In particular, the **positive predictive value of two consistently reactive screening tests is still so low** that it is imperative that further confirmation diagnostics, as described above, be made. However, using two high-sensitivity screening tests, **the negative predictive value is very high with discrepant test results**, especially in low-risk populations, such as in pregnant screenings."*

Both PPV and NPV can be calculated on the basis of values of the WHO itself, see Appendix I. The NPV (Negative Predictive Value) is high enough, even with one negative test result (*discrepant test results*) to safely exclude the "*disease*", while the PPV (Positive Predictive Value) is so low that 2 positive screening results are not enough, but further confirmatory diagnostics are needed.

This will be PCR (also called NAT), see below.

But even if a test should be positive. This only means that one has found fragments of supposed antibodies for the so-called HI virus. But that is

a) not sufficient to confirm the presence of a virus (e.g. HERV)
b) far from the question of whether the suspected virus also causes AIDS. Here, much more speaks against it than for it.

I strongly doubt the medical value of these HIV tests. To me it seems more like a kind of *trawling for candidates*. Once you have found the candidate, you will find something with "*state-of-the-art technology*". If the candidate is then put on HAART, he or she will shortly after show the *correct symptoms*.

11.2. Other problem factors

Humidity

- Packungsbeilage OneStep HIV 1+2 RapiCard™ InstaTest (Limitations of procedure, Punkt 2)

http://www.rapidtest.com/pdf/HIV_1_2_Serum_Plasma_WB_177575-1-12%2808-15-2015%29.pdf

"As with many very sensitive rapid diagnostic tests, false positive results can occur due to the several reasons, most of which are related but not limited to the quality of the sample and ***exposition of the test to humidity.****"*

Internationally different rules for the interpretation of test results

This circumstance has received little or no attention from those affected in the past. In addition, in times of PCR, physician and labs seem to have thought it unnecessary to take care of the basic tests once the diagnosis has been established. This is also a consequence of the pseudo accuracy of PCR.

Tabelle **43-20** Beurteilung von HIV-1-Western-Blot-Ergebnissen

Organisation	Kriterien für ein positives Western-Blot-Ergebnis
American Red Cross (ACR), Deutsches Institut für Normung (DIN)	Eine oder mehr Banden aus folgenden drei Gruppen: p18, p24, p55 (gag); gp41, gp120, gp160 (env); p31, p51, p65 (env)
Association of State and Territorial Public, Health Laboratory Directors (ASTPHLD), Department of Defense (DOD)	Zwei der folgenden Banden: p24 oder p31 und gp41 oder gp120/gp160
Consortium for Retrovirus Serology Standardization (CRSS)	Zwei oder mehr Banden: p24 oder p31 und gp41 oder gp120/gp160
Food and Drug Administration (FDA)	p24, p31 und gp41 oder gp120/gp160
National Institutes of Health (NIH)	p24 und gp41
World Health Organization (WHO)	Mindestens zwei Envelope-Banden (gp160, gp120, gp41)

1699

(from *Lothar Thomas - Labor und Diagnostik*, http://docdro.id/AWNfVdq)

But in fact, even for the basic confirmatory test, the Western Blot Test, it is not agreed on which bands are actually needed to have a positive result, see above, Lothar Thomas - Laboratory and Diagnostics. PCR does not help here because PCR requires that the HIV infection has been confirmed before, see below.

Note: The ELISA test (Enzyme-linked Immunosorbent Assay) starts from a mixture and tries to detect a reaction from the mixture, here the presence of fragments of HIV antibodies or antigens. In the Western blot test, the mixture is additionally split by weight and individual bands are generated. Each band for a protein (p) or glycoprotein (gp) corresponds to the corresponding weight (number), e.g. p24 or gp120 to a molecular weight of 24 and 120 kD (kilodaltons), respectively.

It also seems that the physician, let alone the patient, is not told or presented with the pattern of the bands. This is very worrying, because not only the necessary bands for a positive result are not uniformly defined. The bands also develop in different strength and clarity. Some bands are strong, others only weak. This can also lead to the result "*indeterminate*". With subsequent diagnosis by PCR?

In the end, the lab technician decides which band pattern and band strength of the Western blot test he or she considers sufficient for a HIV+ diagnosis. This corresponds to the training documents of the US Department of Health CDC, cf.

- CDC, Case Studies in Applied Epidemiology, **2003**, No. 871-703, „*Screening for Antibody to the Human Immunodeficiency Virus - Student's Guide*”, https://www.cdc.gov/eis/casestudies/XscreeningHIV.student.871-703.pdf

“*Establishing the cutoff value to define **a positive test result from a negative one is somewhat arbitrary**.“*

It is to be feared that presumed patterns play a role in the diagnosis, e.g. "*poor and from Africa equal to HIV*" or "*male and homosexual equals HIV*".

Comments on cross reactions

- Cross reactions in pregnancies are particularly critical because treatment always affects the child. In addition, it particularly concerns the "*women's problem*" (Annex I). In Germany, HIV is 4 - 5 times less prevalent in women than in men.

- The large number of cross-reactions, the large time frame and the broad geographic distribution make batch problems (manufacturing errors in individual lots) unlikely.

- Cross reactions also occur in tests of the last generation (4th generation).

- Cross reactions also play an important role, as many patients from high-risk groups suffer from classical infections (syphilis, herpes, hepatitis B, influenza, malaria).

- Cross-reactions to tuberculosis, leprosy, malaria or parasites play an important role for developing countries (including Africa) due to the often precarious hygienic situation and the water situation

(parasites).

- Cross-reactions of placental tissue and HIV antibody responses of HERV have long been known to researchers. The reversal seems generally accepted that HIV-positive tissue shows stronger HERV activities. The question may be what does HIV-positive mean in tissue with strong HERV activity?

What can be the causes of these numerous cross reactions?

a) The HIV antibody tests are a bet that research and industry know enough about antibodies to test on it. This is questionable in view of the millions of different antibodies that a human carries in the body, cf. Alberts et al. *Molecular Biology of the Cell*, 4th Ed. https://www.ncbi.nlm.nih.gov/books/NBK26860/

The immune system of humans is permanently active and produces new antibodies and this in great variety, depending on the antigen, which triggers an immune response.

b) There seems to be a fundamental problem in the production and supply of antibodies. The supply is not very reliable:

- Voskuil , "*The challenges with the validation of research antibodies*", F1000Research **2017**, 6:161, Mar **2017**, https://f1000research.com/articles/6-161/v1

A „***reproducibility crisis in biomedical science***" does not sound good.

"*Everyone agreed that to some extent bad quality antibodies may contribute to lack of scientific progress and that something had to be done to remove such blame from the industries.* ***The strong message is that antibodies need proper validation first before being used in scientific research****."*

This influences both the development of antibody tests and their verification.

c) It is **never detected the virus itself**, but only protein fragments, which should have been formed in response to a viral infection (fragments of antibodies). Even the human antibodies against HIV, which are to be proven in the test, are not as specific, as is often assumed.

d) Unspecific antigen / antibody reactions can also have a purely natural origin and lie in the "*nature of the matter*". Unspecific antibodies are a selection advantage and thus favored by evolution until the autoimmune limit (attack of the body's own cells) is reached, cf.

- Marchalonis et al. „*Exquisite specificity and peptide epitope recognition promiscuity, properties shared by antibodies from sharks to humans.*" J. Mol. Recognition, Vol. 14(2), March/17 April **2001**, Pages 110-121, https://onlinelibrary.wiley.com/doi/pdf/10.1002/jmr.527

As a consequence, it is to be feared that in non-risk groups people will be selected who are able to produce antibodies particularly well and perhaps for that very reason.

11.3. Antibody tests - manufacturer's statements

What do the manufacturers say? Everything great? Unfortunately no, because evidently no one can prove HIV. Here are the statements of the manufacturers from the package inserts to HIV Ag / Ab tests:

Alere Determine™ HIV–1/2 Ag/Ab Combo
https://www.fda.gov/media/86959/download

LIMITATIONS of the TEST, Punkt 8
*„A person who has HIV -1 p24 antigen or antibodies to HIV-1 or HIV-2 is **presumed** to be infected*"

BioPlex 2200 HIV Ag-Ab assay
https://www.fda.gov/media/92862/download

LIMITATIONS OF THE PROCEDURE, Punkt 4
"*Reactive specimens must be investigated by additional, **more specific supplemental tests***."

Uni-Gold™ Recombigen® HIV
https://www.fda.gov/media/114893/download

LIMITATIONS, Punkt 5

"*A Reactive result by Uni-Gold Recombigen HIV-1/2 **suggests the presence** of anti-HIV-1 and/or HIV-2 antibodies in the specimen."*

INSTI™ HIV-1/HIV-2 Antibody Test
https://www.fda.gov/media/79719/download

LIMITATIONS OF THE TEST, Punkt 7

"*Because a variety of factors may cause non-specific reactions, a patient found to be Reactive using the INSTI™ HIV-1/HIV-2 Antibody Test should have a blood specimen drawn for **laboratory-based confirmatory testing**."*

DPP® HIV 1/2 Assay
https://www.fda.gov/media/84916/download

LIMITATIONS OF THE PROCEDURE, Punkt 9
*"… the REACTIVE test result is interpreted as **Preliminary Positive** for HIV-1 and/or HIV-2 antibodies."*

Chembio SURE CHECK HIV 1/2
https://www.fda.gov/media/73217/download

LIMITATIONS OF THE PROCEDURE, Punkt 8

*"A Reactive Test Result using the Chembio SURE CHECK HIV 1/2 test **suggests the presence** of antibodies to HIV-1 and/or HIV-2 in the specimen."*

LIMITATIONS OF THE PROCEDURE, Punkt 10

*"A person who has antibodies to HIV-1 or HIV-2 is **presumed to be infected** with the virus."*

ARCHITECT HIV Ag/Ab Combo Reagent Kit (Abbott)
https://www.fda.gov/media/79057/download

*"However, as with all immunoassays, the ARCHITECT HIV Ag/Ab Combo assay may yield **nonspecific reactions due to other causes, particularly when testing in low prevalence populations.** A repeatedly reactive specimen* **should be investigated further with supplemental confirmatory HIV-specific tests***, such as immunoblots, antigen tests, and HIV nucleic acid tests."*

Genscreen HIV Combo Ag/Ab EIA (Bio-Rad)
https://www.fda.gov/media/81553/download

LIMITATIONS OF THE PROCEDURE (Punkt 13)
"*Repeatedly reactive specimens must be investigated **by additional, more specific, or supplemental tests**."*

*"A person who has antibodies to HIV is **presumed to be infected** with the virus,…".*

HIV Ag/Ab Combo (CHIV) Assay (SIEMENS ADVIA Centaur)
https://www.fda.gov/media/92283/download

LIMITATIONS
"*Patients routinely exposed to animals or to animal serum products for diagnosis or therapies can be prone to this interference and anomalous values may be observed. **Specimens from patients who have received mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies and may interfere in assays that employ mouse monoclonal antibodies.***"

"*A person who has antigen or antibodies to HIV is **presumed to be infected** with the virus."*

Abbot Labs HIVAB HIV-1/HIV-2 (rDNA) EIA

https://www.fda.gov/media/73256/download

*„At present, there is **no recognized standard for establishing the presence or absence of antibodies to HIV-1 and HIV-2** in human blood."*

MedMira Reveal Rapid HIV -1 Antibody Test

https://www.fda.gov/media/73550/download

"A Reactive test result using the Reveal™ Rapid HIV -1 Antibody Test ***suggests the presence of anti-HIV-1 antibodies*** *in the specimen*."

Genetic Systems HIV-1/HIV-2 PLUS O EIA

https://www.fda.gov/media/73524/download

"A person who has antibodies to HIV-1 is ***presumed to be infected*** *with the virus,.. ."*

Elecsys HIV combi PT

https://www.fda.gov/media/105906/download

Limitations of the test

"A person who has antigen or antibodies to HIV ***is presumed to be infected*** *with the virus."*

Comments on the manufacturer's statements

Although some manufacturers promise a sensitivity or specificity close to 100% or even 100%: a failure to reach the specified limits would have no consequences for them. **None of the tests guarantees the results**. The manufacturers say that they detect HIV antibodies (or an HIV antigen) that **suggest** HIV infection, but this has **to be confirmed in the laboratory**.

The more, as is shown in Annex I even a specificity close to 100% does not lead to a positive predictive value greater than 1%. That has to do with the low prevalence of the HI virus. That means that a lot of false positive tests are to be expected.

Manufacturers say they only provide a positive candidate for further investigation. But **100% candidate makes no sense**, especially because of the problems with PCR, see below.

The fear is that the candidates expect months-long series of tests, which, however, in part due to lack of true infection, provide no clear results (see below). For how many candidates will you undertake this effort? And what does that mean for statistics, e.g. from Africa?

That is a bit strange. I would have expected that after a positive test at least the result is certain. But it is probably only intended as an introduction to further tests. How long does a "*patient*" endure this?

But what about PCR? It is always said that PCR is so incredibly sensitive that single molecules can be detected. But here too, the manufacturers keep a low profile.

11.4. PCR confirmatory tests - manufacturer's statements

PCR can certainly test the presence of individual molecules. But that says nothing about whether this molecule was already present in the original medium (contamination) or whether the presence leads to a pathogenic effect. But what do manufacturers say about PCR testing?

It is little-known that in the package leaflet of PCR test assays it is stated that the HIV infection must have been established before, cf.

Roche AMPLICOR HIV-1 MONITOR Test
https://www.fda.gov/media/73854/download

*„The AMPLICOR HIV-1 MONITOR Test is **not intended to be used as a screening test for HIV or as a diagnostic test** to confirm the presence of HIV infection."*

COBAS® AmpliScreen HIV-1 Test, version 1.5
https://www.fda.gov/media/73991/download

"*The COBAS® AmpliScreen HIV-1 Test, v1.5 may **not be used to replace HIV-1 antibody detection tests** such as EIA or Western Blot."*

COBAS AmpliPrep/COBAS TaqMan HIV-1 Test
https://www.fda.gov/media/73832/download

*"The COBAS AmpliPrep/COBAS TaqMan HIV-1 Test is **not intended to be used as a screening test for HIV or as a diagnostic test** to confirm the presence of HIV infection."*

COBAS TaqScreen MPX Test, version 2.0
https://www.fda.gov/media/90540/download

*"This test is **not intended for use as an aid in diagnosis of infection with HIV**, HCV, or HBV."*

VERSANl HIV-1 RNA 3.0 Assay (bDNA)
https://www.fda.gov/media/73497/download

*„The VERSANT HIV-1 RNA 3.0 Assay (bDNA) is **not intended for use as a screening assay for HIV infection or as a diagnostic test** to confirm the diagnosis of HIV infection*".

Aptima HIV-1 Quant Assay (Hologic)
https://www.fda.gov/media/102425/download

"*This assay is **not intended to be used as a donor screening test for HIV-1 or as a diagnostic test** to confirm the presence of HIV-1 infection.*"

Abbott RealTime HIV-1
https://www.fda.gov/media/73278/download
INTENDED USE

"*This assay is **not intended to be used as a donor screening test for HIV-1 or as a diagnostic test** to confirm the presence of HIV-1 infection.*"

Procleix Ultrio Elite Assay
https://www.fda.gov/media/112861/download

"*This assay is **not intended for use as an aid in diagnosis of infection with HIV-1, HIV-2**, HCV or HBV.*"

NucliSens HIV-1 QT — HIV QT
https://www.fda.gov/media/73107/download

*"The NucliSens® HIV-1 QT assay **is not intended to be used as a screening test for HIV-1 nor is it to be used as a diagnostic test to confirm the presence of HIV-1 infection**."*

Comments on PCR confirmatory tests

What is it? Questionable antibody tests on protein fragments with numerous cross-reactions as a prerequisite but also as the confirmation of even more questionable PCR RNA / DNA fragment analysis? It pays off to continue with PCR and to shed some more light on this method. The thread is a medical apparatus in which the diagnosis is detached and outsourced to machines and the results may not be questioned.

The problem with PCR is that the test does not test for the RNA or DNA of the whole gen of the protein molecule, which comprises some 1000 amino acids, thus times 3x bases, but actually 20-40 base pairs of the RNA or DNA. These 20-40 base pairs are called "*primers*", actually correspond to about 10 amino acids (instead of 1000) and these 20-40 bases decide what is detected by PCR. This leads to significant problems with false positives.

But before we go back once more to the *Gemeinsamen Diagnostikkommission der Deutschen Vereinigung zur Bekämpfung von Viruskrankheiten e. V. (DVV e. V.) und der Gesellschaft für Virologie e. V. (GfV e. V.)*

Translation

„Joint Diagnostic Commission of the German Association for the Control of Viral Diseases e. V. (DVV e.V.) and the Society for Virology e. V. (GfV e.V.)“

This commission also has something to say about PCR and in particular to the question of how physicians should behave when they use PCR for diagnosis, although manufacturers reject this, cf.

- Rabenau et al., *„Nachweis einer Infektion mit Humanem Immundefizienzvirus (HIV): Serologisches Screening mit nachfolgender Bestätigungsdiagnostik durch Antikörper-basierte Testsysteme und/oder durch HIV-Nukleinsäure-Nachweis“*, Bundesgesundheitsbl **2015** · 58:877–886, http://www.dvv-ev.de/news/HIV-Diagnostik_Bundesgesundheitsblatt_2015.pdf;jsessionid=9953B353E4D1AAB755F015F7F10D0F31.2_cid298.pdf

Translation

“Federal Health Bulletin”

„Detection of Human Immunodeficiency Virus (HIV) Infection: Serological Screening with Subsequent Confirmatory Diagnosis by Antibody-Based Assay Systems and / or by HIV-Nucleic Acid Detection“

Well. You write it down. Then you have it in writing.

p. 879

*„Werden im Rahmen der Stufendiagnostik NAT zum Nachweis einer HIV-Infektion verwendet, müssen sowohl der vom **Testhersteller vorgegebene Verwendungszweck** als auch die Art der primär gewonnenen Probe beachtet und ggf. **im Befund kommentiert werden** (siehe Anlage D).“*

Translation

*„If NAT is used for the detection of HIV infection in the step diagnostics, both **the purpose specified by the test manufacturer** and the type of primary sample must be taken into account and, if necessary, **commented on in the report** (see Annex D).“*

p. 879

*„Die Mehrzahl der kommerziellen HIV-1-NAT-Systeme ist von den Herstellern bislang nur für den Einsatz im Kontext einer HIV-Therapie (Therapiemonitoring) vorgesehen („Companion testing“). Die Anwendung von HIV-NAT-Systemen für den Erstnachweis einer HIV-Infektion im Rahmen der Stufendiagnostik ist möglich, **sollte jedoch im Befund kommentiert werden**.“*

Translation

*„The majority of commercial HIV-1 NAT systems have been provided by manufacturers so far only for use in the context of HIV therapy (therapy monitoring) ("companion testing"). The use of HIV-NAT systems for the first detection of HIV infection in the context of stage diagnostics is possible, **but should be commented on in the findings.**“*

p. 885 – Formulation proposal for the findings text

„Der verwendete HIV-NAT ist vom Hersteller für die Verlaufsdiagnostik bei bekannter HIV-Infektion, aber nicht für den Erstnachweis einer HIV-Infektion vorgesehen. ***Der Einsatz der HIV-NAT im Rahmen der Stufendiagnostik entspricht jedoch den aktuellen Empfehlungen zur HIV-Bestätigungsdiagnostik****"*.

Translation

„The HIV-NAT used by the manufacturer is intended for the follow-up diagnosis of known HIV infection, but not for the first detection of HIV infection. ***However, the use of HIV-NAT as part of the step-by-step diagnosis is in line with the current recommendations for HIV confirmatory diagnostics****."*

In summary, we can recall the recommendations of the DVV in the *Federal Health Bulletin* (see above for HIV screening tests):

- The PPV of HIV screening tests is so low that 2 positive tests are not sufficient. Further confirmatory diagnostics is required.

- PCR (NAT) is not intended for diagnosis according to the manufacturer. But: we recommend it anyway and with that it is permissible.

Should we not expect that a methodology for therapy monitoring is also suitable for diagnosis? Or does the diagnosis then no longer matter? It's the same game as with the antibody tests. No one can prove anything. That is not needed. The consensus of the so-called experts in cooperation with the industry is enough. At any rate, that should not be called science. It's good for the business. But it certainly is not in the patient's interest.

The caution of the manufacturer is no coincidence. What happens is, in my opinion, the following. The many false positives in serological HIV Ag / Ab testing (see above) indicate that there are systematic problems with the diagnosis by these biomarkers. It can very well be that a positive HIV Ag / Ab test is a sign (biomarker) for a stressed body. This would correspond to the situation in risk groups (infections, drugs, ..) and also in large parts of Africa (malnutrition, heavy metal poisoning, parasites, classical epidemics, ...).

In addition, in case of PCR, one tests for short genetic sequences of the putative HI virus (so-called primers, see below), but these sequences are constantly changing as the putative HI virus appears to mutate frequently, i.e. a spontaneous change in the genetic sequence occurs. Cf.

- Cuevas et al., "*Extremely High Mutation Rate of HIV-1 In Vivo*", Published online **2015** Sep 16, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4574155/

"This reveals an extremely high mutation rate of $(4.1 \pm 1.7) \times 10^{-3}$ *per base per cell,* ***the highest reported for any biological entity.****"*

This seems to me the reason that manufacturers demand that a suspected HIV infection must be established beforehand and that PCR is not suitable for initial diagnosis. In the last 25 years, so many putative HI virus sequences have been put into the gene databases (see below) that it would probably be enough for hundreds of viruses. But which of them would be selective for the individual and which correspond to

natural gene sequences, e.g. of bacteria that naturally populate the human body? But again in each person differently.

The assumption that one is dealing with a mutation in any case may seem plausible, but it is by no means compulsory, just to think of endogenous retroviral components, which are also different in every human being. But, with thousands of different gene sequences attributable to the HI virus, you will always find something **if you assume an infection**. Which person has the nerve strength to survive this procedure unscathed?

These are classic circular statements that make up the bulk of these diagnostic protocols. In my opinion, completely irresponsible. But, the industry is here spotlessly clean. Thanks to the consensus commissions of the so-called experts.

I strongly assume that the essential part of the diagnosis comes from the patient's information and the personal impression. Does the person indicate having had risky sexual contacts or is this person recognizably from a risk group so the diagnosis in case of doubt will be *HIV+*.

12. False positives in PCR and the diagnosis of retroviral activity

PCR or what is actually in the test tube? Here one tricked the population a pseudo accuracy. Even worse, in the presence of antibodies in the human body, the presence of a molecule (or 50 molecules per ml) does not say anything about whether it is a pathogenic, i.e. causes a disease.

Since most of us had chickenpox, we should all have shingles when it comes to PCR. That's obviously not the case. Of course, there is shingles and it is caused by the chickenpox virus. But people are not treated for a lifetime against chickenpox.

However, this seems sufficient for these serious cell toxins in HIV therapy (HAART).

PCR can detect very sensitively the presence of certain RNA or DNA fragments in the medium. But it can neither make any statement about the bioactivity of inactive i.e. latent viruses, nor the pathogenicity. The pathogenicity must be known beforehand. Thus, PCR does not differentiate between correlation and causality.

Note: For PCR short DNA pieces are needed, so-called primers, cf. https://en.wikipedia.org/wiki/Primer_(molecular_biology). These primers are not very long, about 20-40 base pairs (bp). The sequence of base pairs is chosen so that it is complementary to a putative pathogen DNA and can dock to a present DNA (template) in the medium. The DNA polymerase in the medium then extends the primers and creates a double strand along the single strand template. These steps are repeated several times and at each step the existing DNA material doubles. For the procedure cf. also http://www.aun.edu.eg/molecular_biology/PCR(1)/Primer%20Design.pdf

Obviously, the specificity of the primers is of considerable importance in this detection method. In a significant number of cases it comes to false positives. This has its cause on the one hand in "*impurities*" in the medium. No one knows exactly what is really in the test tube, see also Appendix II. On the other hand, the primers are not as specific as you would like.

Cf. false HIV positives in PCR:

- Busch et al., "*Poor sensitivity, specificity, and reproducibility of detection of HIV-1 DNA in serum by polymerase chain reaction. The Transfusion Safety Study Group*.", J Acquir Immune Defic Syndr. **1992**;5(9):872-7, https://www.ncbi.nlm.nih.gov/pubmed/1512686

*"HIV-1 gag signal was also reported for 28 of 151 PCR determinations on **34 samples from noninfected blood donors (18.5% false-positive rate)**."*

*"These results indicate that current techniques for detecting cell-free HIV-1 DNA in serum **lack adequate sensitivity, specificity, and reproducibility for widespread clinical applications**."*

These findings do not seem to have bothered anyone. The method was used contrary to the manufacturer's statements for diagnosis and *refined* on living object.

- De Mendoza et al., *"False positive for HIV using commercial viral load quantification assays."*, AIDS **1998**. 12:2076-2077, https://www.ncbi.nlm.nih.gov/pubmed/9814879

- Rich et al. "*Misdiagnosis of HIV infection by HIV-1 plasma viral load testing: A case series.",* Ann Intern Med **1999**. 130:37-39, https://www.ncbi.nlm.nih.gov/pubmed/9890848

"Infection with HIV was initially diagnosed in all three patients, but each patient subsequently tested negative by HIV-1 enzyme-linked immunosorbent assay and repeated plasma viral load testing."

- Bakshi et al., "*Repeatedly positive human immunodeficiency virus type 1 DNA polymerase chain reaction in human immunodeficiency virus-exposed seroreverting infants*.", Pediatr Infect Dis J. **1995** Aug;14(8):658-62, https://www.ncbi.nlm.nih.gov/pubmed/8532421

- Feucht et al. „*False-positive HIV DNA PCR testing of infants: Implications in a changing epidemic*", March **2012**, Vol. 102, No. 3, SAMJ, https://www.ncbi.nlm.nih.gov/pubmed/22380909

- Jagtap et al. "*Discordant HIV DNA PCR results among infants diagnosed with HIV infection and initiated on ART: a case series.*", Int J STD AIDS. **2017** Mar;28(4):415-417, https://www.ncbi.nlm.nih.gov/pubmed/27638411

- De Ravin et al. "*False-Positive HIV PCR Test Following Ex Vivo Lentiviral Gene Transfer Treatment of X-linked Severe Combined Immunodeficiency Vector*.", Mol Ther. **2014** Feb; 22(2): 244–245, https://www.ncbi.nlm.nih.gov/pubmed/24487563

- Mathai et al. "*Repeated false positive HIV DNA PCR in an exposed infant*", Med J Armed Forces India. **2013** Oct; 69(4): 392–393, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3862937/

- Havlichek et al. "*False-positive HIV diagnosis by HIV-1 plasma viral load testing*.", Ann Intern Med. **1999** Nov 16;131(10):794, https://www.ncbi.nlm.nih.gov/pubmed/10577313

- Kiely et al., "*The potential complexity and need for caution when interpreting atypical human immunodeficiency virus reactivity in blood donors*.", Blood Transfus. **2015** Oct; 13(4): 669–671, https://www.ncbi.nlm.nih.gov/pubmed/26192776

"*However, over the 17-month follow-up period,* ***while all samples remained strongly reactive on the anti-HIV immunoassays, there was no progression to a western blot-positive result.*** *HIV RNA was not detected in any of the donor's samples tested at VIDRL on the Abbot Real Time or Roche Taqman assays, despite replicate testing on the Roche assay on two occasions. In addition, three samples were tested for proviral DNA and all three were negative. After the 17-month follow-up period, which included both laboratory testing and clinical assessment, the donor's results were assessed as not consistent with HIV infection.* ***Given***

this assessment, the discordant results for the Ultrio Plus and dHIV assays could be due to contamination or represent false positive results but we were unable to distinguish between these two explanations.*"*

- Quirós et al., "*Diagnosis of HIV-1 infection by PCR with two primer pairs*.", Eur J Epidemiol. **1993** Jul;9(4):426-9, https://www.ncbi.nlm.nih.gov/pubmed/8243598

"…, in the ***seronegative*** *at risk group 2 samples were positive with only one primer pair (SK38/SK39), and* ***4 samples were found positive by both primer pairs*** *(SK38/39 & SK68/69)."*

- Kakaiya et al., "*False-positive nucleic acid test results for human immunodeficiency virus RNA and hepatitis C virus RNA: an underappreciated problem*." Transfusion. **2011** Jan;51(1):225-6, https://www.ncbi.nlm.nih.gov/pubmed/21219326

- Agarwal et al., "*False positive HIV-1 DNA PCR in infancy.*", Indian Pediatr. **2008** Mar;45(3):245-6, https://www.ncbi.nlm.nih.gov/pubmed/18367778

"*Surprisingly, all 3 PCR positive neonates were non-reactive to ELISA*."

The situation is further complicated by the fact that patients often suffer from classical infections, especially in developing countries, tuberculosis and malaria are common. It is tested until something is found. Woe to those who get into these diagnostic mills, cf.

- Debyser et al. "*Failure to quantify viral load with two of the three commercial methods in a pregnant woman harboring an HIV type 1 subtype G strain*.", AIDS Res Hum Retroviruses. **1998** Mar 20;14(5):453-9, https://www.ncbi.nlm.nih.gov/pubmed/9546805

"*We investigated the discrepant observation of an undetectable viral load in an immunodeficient pregnant HIV-1-infected patient of African origin with no prior antiretroviral treatment. Although clinical progression was present in this patient with* ***tuberculosis and a low CD4 cell count, viral load determinations with both the Amplicor Monitor and NASBA assays revealed no detectable RNA levels.***"

Is the methodology developed at the living object? It seems that only one thing cannot happen: that the patient simply suffers from tuberculosis, which is usually curable.

- Oberhelman et al., "*A Controlled Study of Tuberculosis Diagnosis in HIV-Infected and Uninfected Children in Peru*", PLoS ONE, **2015** Apr 30 10(4): e0120915, https://www.ncbi.nlm.nih.gov/pubmed/25927526

„The inadequacy of these PCR results only became apparent because well-controls were included in similar numbers to cases, in contrast to many previous studies of pediatric TB diagnostics "

„PCR sensitivity was difficult to assess because ***false-positives were more common than true positives****."*

Today PCR assays are tested often only against each other, presumably because there is no standard. That does not seem sufficient. I think that here is a basic problem in the diagnosis of retroviral activities.

This is supported by the fact that a very high correlation between DNA sequences isolated from **breast cancer and prostate cancer patients on the one hand, and HIV on the other hand** has been found.

That seems somewhat surprising. In order to explain:

In the late 1990s, Rakowicz-Szulczynska et al. isolated HIV-1 DNA sequences from breast and ovarian cancer tissue. Breast cancer tissue DNAs from 40 patients were amplified using HIV-1 env (gp41) primers and all samples were positive. DNA fragments amplified in seven randomly selected breast cancer samples were sequenced, i.e. the base sequence of the DNA was analyzed. Over a length of 141-143 base pairs (bp), the sequences from the breast cancer cells coincided with 90-95% agreement with a segment of HIV-1, group M, and subtype B, the major HIV-1 subtype. This subtype is prevalent in the US, Western Europe and Australasia. Rakowicz-Szulczynska et al. reported similar findings in ovarian and prostate cancer, cf.

- Rakowicz-Szulczynska et al., *"Human immunodeficiency virus type 1-like DNA sequences and immunoreactive viral particles with unique association with breast cancer."* Clinical and Diagnostic Laboratory Immunology **5**, 645-53 (**1998**), https://www.ncbi.nlm.nih.gov/pubmed/9729531

*"The **average similarity to HIV-1 in all of the breast cancer DNAs tested was at least 90%** (Fig. 4), which indicated a strong homology of the identified cancer sequences to HIV-1."*

- Rakowicz-Szulczynska et al., "*Prostate, breast and gynecological cancer markers RAK with homology to HIV-1.*", Cancer Letters **124**, 213-23 (**1998**), https://www.ncbi.nlm.nih.gov/pubmed/9500213

"The DNA fragments amplified in prostate cancer and in BPH showed more than 90% homology to the HIV-1 gene for gp41."

- Rakowicz-Szulczyn et al. " *Relevance of the Viral RAK Alpha Gene in Diagnosis of Malignant Versus Nonmalignant Tumors of the Ovary and Uterus*", Clin Diagn Lab Immunol. **2000** May; 7(3): 360–365, https://www.ncbi.nlm.nih.gov/pubmed/10799446

„*The RAK alpha gene was PCR amplified with HIV-1-derived primers SK68 and SK69. RAK antigens p120, p42, and p25* ***were found in 95% of ovarian, uterine, and cervical cancer cases and in 75% of vulvar cancer cases***."

"***DNA sequences amplified in all cancer cases exhibited more than 90% homology to HIV-1 gp41*** *and were encoded for the functional peptide*."

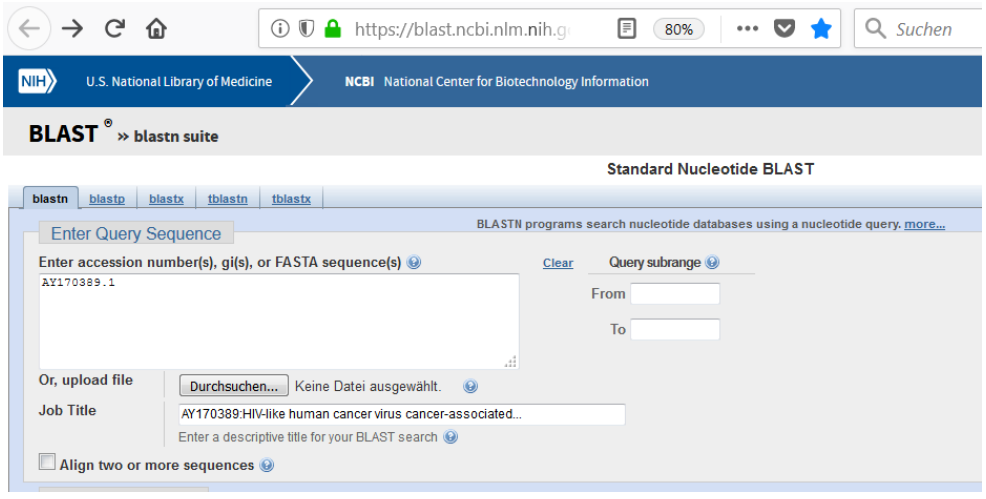
These analyzes can be understood by carrying out a corresponding query in the BLAST gene database. To do this, one takes the gene sequence of Rakowicz-Szulczynska et al. which is stored under http://www.ncbi.nlm.nih.gov/nuccore/?term=(Rakowicz-Szulczynska)+AND+%22HIV-like+human+cancer+virus%22%5Bporgn%3A__txid433832%5D , e.g.

The base sequence for "***HIV-like*** *human cancer virus cancer-associated protein RAK alpha (RAK alpha) gene*" (Accession Number: AY170389.1) is:

"GCAGCAGGAAGCACTATGGGCGCAGCGTCAATAACGCTGACGGTACAGGCCAGACAATTGTTGTCTGGTATAGTGAA ACAGCCAAACAATTTGCTGAGGGCTATTGATGCGCAACAGCTTCTGTTGCAACTCACAGTCTGG"

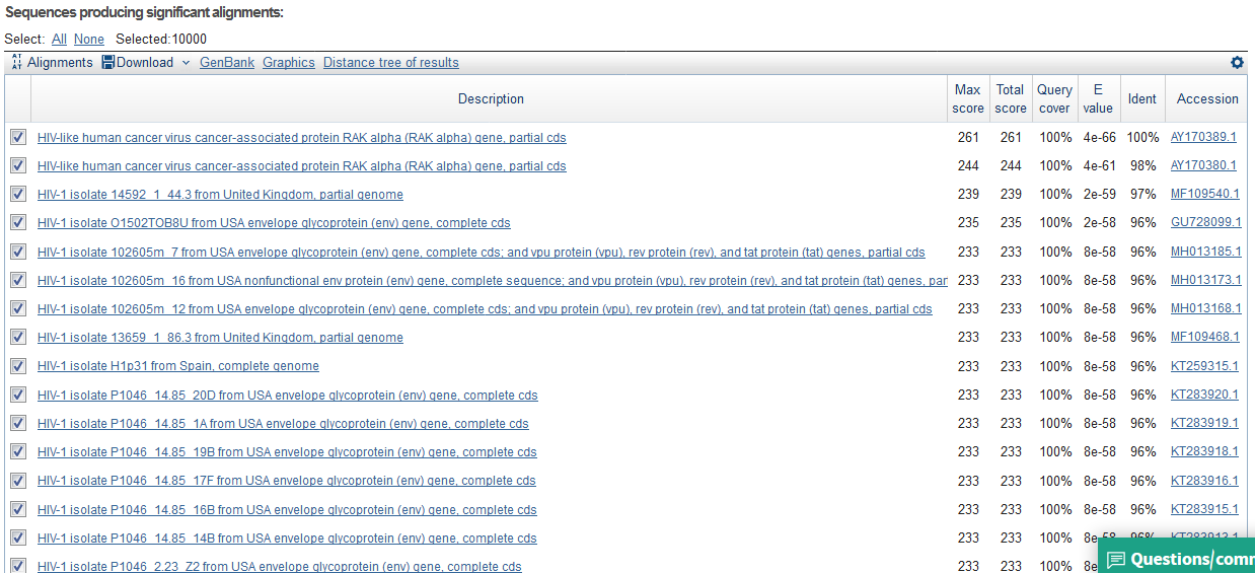
This is the gene sequence that Rakowicz-Szulczynska et al. have isolated from breast cancer patients.

By entering the accession number, here AY170389.1, in https://blast.ncbi.nlm.nih.gov/Blast.cgi?PAGE_TYPE=BlastSearch, you can search for homologous sequences:



Press BLAST, if necessary increase the number of displayed hits under Algorithmic Parameters:

The database now searches in all stored gene sequences for matching base sequences that correspond to the entered sequence. The result list is as follows:



Sequences producing significant alignments:

Select: All None Selected:10000

Alignments Download GenBank Graphics Distance tree of results

Description	Max score	Total score	Query cover	E value	Ident	Accession
HIV-like human cancer virus cancer-associated protein RAK alpha (RAK alpha) gene, partial cds	261	261	100%	4e-66	100%	AY170389.1
HIV-like human cancer virus cancer-associated protein RAK alpha (RAK alpha) gene, partial cds	244	244	100%	4e-61	98%	AY170380.1
HIV-1 isolate 14592_1_44.3 from United Kingdom, partial genome	239	239	100%	2e-59	97%	MF109540.1
HIV-1 isolate O1502TOB8U from USA envelope glycoprotein (env) gene, complete cds	235	235	100%	2e-58	96%	GU728099.1
HIV-1 isolate 102605m_7 from USA envelope glycoprotein (env) gene, complete cds; and vpu protein (vpu), rev protein (rev), and tat protein (tat) genes, partial cds	233	233	100%	8e-58	96%	MH013185.1
HIV-1 isolate 102605m_16 from USA nonfunctional env protein (env) gene, complete sequence; and vpu protein (vpu), rev protein (rev), and tat protein (tat) genes, par	233	233	100%	8e-58	96%	MH013173.1
HIV-1 isolate 102605m_12 from USA envelope glycoprotein (env) gene, complete cds; and vpu protein (vpu), rev protein (rev), and tat protein (tat) genes, partial cds	233	233	100%	8e-58	96%	MH013168.1
HIV-1 isolate 13659_1_86.3 from United Kingdom, partial genome	233	233	100%	8e-58	96%	MF109468.1
HIV-1 isolate H1p31 from Spain, complete genome	233	233	100%	8e-58	96%	KT259315.1
HIV-1 isolate P1046_14.85_20D from USA envelope glycoprotein (env) gene, complete cds	233	233	100%	8e-58	96%	KT283920.1
HIV-1 isolate P1046_14.85_1A from USA envelope glycoprotein (env) gene, complete cds	233	233	100%	8e-58	96%	KT283919.1
HIV-1 isolate P1046_14.85_19B from USA envelope glycoprotein (env) gene, complete cds	233	233	100%	8e-58	96%	KT283918.1
HIV-1 isolate P1046_14.85_17F from USA envelope glycoprotein (env) gene, complete cds	233	233	100%	8e-58	96%	KT283916.1
HIV-1 isolate P1046_14.85_16B from USA envelope glycoprotein (env) gene, complete cds	233	233	100%	8e-58	96%	KT283915.1
HIV-1 isolate P1046_14.85_14B from USA envelope glycoprotein (env) gene, complete cds	233	233	100%	8e-58	96%	KT283913.1
HIV-1 isolate P1046_2.23_Z2 from USA envelope glycoprotein (env) gene, complete cds	233	233	100%	8e		

Questions/comm

The results list shows > 1000 hits from HIV-1 proteins with > 95% identical primary structure and that for a DNA sequence isolated from breast cancer cells.

The problem seems to have been that for the last 25 years, a completely HIV-centric research has dominated and everything that was found in connection to HIV has been stored in the gene databases. As one could see above, these were not all HIV+ humans. Moreover, nobody knows what PCR has enhanced, because nobody knows exactly what was in the medium. For PCR this must be clear down to the last molecule.

The following finding, which found a significant match between HIV gene sequences and a whole series of naturally occurring organisms as well as human DNA in a search in the BLAST gene database, also supports this interpretation.

- Romero, *„Contamination of genomic databases by HIV-1 and its possible consequences. A study in Bioinformatics.“*, March **2014**, http://openaccess.uoc.edu/webapps/o2/bitstream/10609/31361/1/Contamination_of_genomic_databases_by_HIV-1_Bioinformatic.pdf

In essence, the query is analogous to the above. There are "*known*" HIV gene sequences entered into the query and it is looked at what else can be found. To me it seems premature to talk about contamination of the database, but anything else would probably not be published currently.

Extract from Romero, *„Contamination of genomic databases by HIV-1 and its possible consequences. A study in Bioinformatics.“*, March **2014**:

„A 67 bp segment of human chromosome 8 DNA that has a 99% (66/67) alignment with HIV-1 DNA between base pairs 6348-6414. This segment is a partial cds for HIV-1 proteins p120 and p160”

Note: *cds* means „*Coding DNA sequence*“, cf. https://en.wikipedia.org/wiki/Coding_region.

Table 4: TBLASTN HIV-1 amino acid sequences identity search against specified taxa

Sequence	Subject (bp)	Cover	Identity	E-Value	Data
HIV p31 (288aa)	*Schistosoma mansoni* (6914)	90%	28%	2e-23	Link 38
HIV p24 (231aa)	*Homo sapiens* chromosome 7, GRCh37.p13 (159138663)	60%	37%	6e-11	Link 39
	Homo sapiens chromosome 3, GRCh37.p13 (198022430)	51%	36%	4e-09	Link 40
HIV p55 (500aa)	*Schistosoma mansoni* (6914)	46%	29%	2e-17	Link 41
HIV p51 (440aa)	*Homo sapiens* genomic sequence surrounding *Not*I site (597)	38%	71%	2e-81	Link 42
	Cryptococcus neoformans var. grubii H99 chromosome 12 (774062)	61%	25%	3e-11	Link 43
	Schistosoma mansoni (6914)	64%	36%	4e-46	Link 44
HIV polPolyprotein (1003aa)	*Homo sapiens* genomic sequence surrounding *Not*I site (597)	16%	71%	4e-78	Link 45
	Candida albicans genomic DNA, chromosome 7 (949626)	46%	29%	1e-09	Link 46
	Homo sapiens chromosome 7, GRCh37.p13 (159138663)	94%	26%	1e-63	Link 47
HIV p41 (345aa)	Uncultured fungus (856)	23%	93%	4e-45	Link 48
HIV p120 (511aa)	Uncultured fungus *(856)*	7%	100%	4e-14	Link 49
HIV p160 (856aa)	Uncultured fungus (856)	14%	93%	1e-53	Link 50
HIV p66 (560aa)	*Homo sapiens* genomic sequence surrounding *Not*I site (597)	31%	68%	7e-81	Link 51
	Schistosoma mansoni (6914)	50%	36%	8e-46	Link 52
	Homo sapiens chromosome 7, GRCh37.p13 (159138663)	99%	28%	2e-48	Link 53

(From Romero, 2014, table 4)

It is not clear how a contamination of a database can occur:

„Notwithstanding, there are several reasons why contamination may not be the universal explanation for these data. They include

(a) there is no actual proof of contamination

(b) sequences are deposited by laboratories conducting research unrelated to HIV

(c) some sequences are reported by laboratories at foremost institutions

(d) laboratories undertake forensic precautions to exclude and neutralise contamination

(e) no HIV-1 DNA alignments were found in the nine sets of "control", 6 non-HIV-RNA virus genomes similar in length to the HIV-1 genome (data not shown)

(f) using the HIV-1 gp41-derived primers SK68 and SK69 HIV-1 sequences were reported in malignant tissues of patients in the absence of HIV-1 infection"

One circumstance that receives little or no attention is the fact that one (!) molecule suffices to initiate the reaction in PCR. These can also be DNA components that have passed from the digestive system into the blood, cf.

- Spisák et al., "*Complete genes may pass from food to human blood.*", PLoS One. **2013** Jul 30;8(7):e69805, https://www.ncbi.nlm.nih.gov/pubmed/23936105

"*Here, based on the analysis of over 1000 human samples from four independent studies, we report evidence that* ***meal-derived DNA fragments which are large enough to carry complete genes can avoid degradation*** *and through an unknown mechanism enter the human circulation system.* ***In one of the blood samples the relative concentration of plant DNA is higher than the human DNA***."

- Schubbert et al., "*Foreign (M13) DNA ingested by mice reaches peripheral leukocytes, spleen, and liver via the intestinal wall mucosa and can be covalently linked to mouse DNA*.", Proc Natl Acad Sci U S A. **1997** Feb 4;94(3):961-6, https://www.ncbi.nlm.nih.gov/pubmed/9023365

"*In 84 animals, fragments of M13mp18 DNA were detected in the contents of the small intestine, the cecum (until 18 h), the large intestine, or the feces. In 254 animals, M13mp18 DNA fragments of up to 976 bp were found in blood 2-8 h after feeding. In buffer-fed control animals, M13mp18 DNA could not be detected.*"

"*M13mp18 DNA could be traced by fluorescent in situ hybridization in the columnar epithelial cells, in the leukocytes in Peyer's patches of the cecum wall, in liver cells, and in B cells, T cells, and macrophages from spleen.* ***These findings suggest transport of foreign DNA through the intestinal wall and Peyer's patches to peripheral blood leukocytes and into several organs***."

It seems that there are significant doubts about the specificity of PCR in this overall data set and that one should not believe everything that comes out of PCR, independent of the question of whether it is pathogenic. **Therefore, it would be wrong to assume a viral mutation in dubious test results and to put simply an adapted primer sequence in the database. Then the diagnostic method would have become completely detached and beyond any control.**

Since in virology HIV research has been funded almost exclusively in the last 25 years, it seems reasonable to assume that it is more the contrary, namely that many gene sequences have been erroneously attributed to HIV, but are now in the database under this name. This is also supported by the following publication,

- Yuan et al., "*It Is Imperative to Establish a Pellucid Definition of Chimeric RNA and to Clear Up a Lot of Confusion in the Relevant Research*.", Int J Mol Sci. **2017** Mar 28;18(4). pii: E714, https://www.ncbi.nlm.nih.gov/pubmed/28350330

"*There* ***have been tens of thousands of RNAs deposited in different databases that contain sequences of two genes and are coined chimeric RNAs, or chimeras. However, "chimeric RNA" has never been lucidly defined****, partly because "gene" itself is still ill-defined and because the means of production for many RNAs is unclear."*

Also this view shines a different light on the supposed high mutation rate of the supposed HI virus.

To summarize: PCR is not only hypersensitive, it cannot detect viral effect under the influence of antibodies *in vivo* and it creates almost any truths, since almost any RNA / DNA fragments can be found without any infection. Also it should be looked at how the measurements develop under HAART, i.e. when taking chain terminators into account that generate any form of DNA fragments, see above.

Added to this is the problem of "*quantitative*" PCR. qPCR supposedly not only determines what is in the medium, but also how much of it. There is considerable doubt that the PCR method is capable of a

reproducible quantitative statement. According to the procedure, the individual molecules are amplified by a factor of about 1,000,000,000x (~=2^{30}) and every error enters exponentially.

What is "*quantitative*" in qPCR, usually refers to the diagnosis only, which according to the manufacturers should not be, and the question of whether any suspected viral fragments can be detected. The absolute viral load is hardly considered, as this number can hardly be reproduced. In a study by the US Department of Health, CDC, samples for qPCR analysis have been sent to various laboratories. The specific suspected viral loads varied by up to a factor of **67x**, cf.

- CDC Morbidity and Mortality Weekly Report, November 16, **2001**, Vol. 50, No. RR-20, https://www.cdc.gov/mmwr/PDF/rr/rr5020.pdf, Tabelle 2

Roche Amplicor HIV-1 Monitor: 71 Labs

Minimum	Median	Maximum
3,849	118,000	259,018

Particularly impressive is the number of laboratories that want to be supplied regularly with patient samples. However, these specialized HIV labs increase the problem of sample contaminations from the previous run. 1 molecule suffices.

Apart from the fact that PCR cannot distinguish between latent and active viruses and apart from the problem of specificity: in comparison to conventional methods, PCR overestimates the concentration of putative viral fragments by up to **60,000x**, cf..

- Piatak et al., "*High Levels of HIV-1 in Plasma During All Stages of Infection Determined by Competitive PCR*", Science. **1993** Mar 19;259(5102):1749-54, https://www.ncbi.nlm.nih.gov/pubmed/8096089

„*Plasma virus levels determined by QC-PCR correlated with,* ***but exceeded by an average of 60,000-fold****, virus titers measured by endpoint dilution culture.*"

How can it be, given the alleged enormous specificity of PCR, that a syphilis infection (very common in HIV+ measured people in risk groups) or worms (very common in Africa) influence the so-called viral load? Cf.

- Buchacz et al, "*Syphilis increases HIV viral load and decreases CD4 cell count*", AIDS **2004**, 18:2075–2079, https://www.ncbi.nlm.nih.gov/pubmed/15577629

- Palacios et al., „*Impact of syphilis infection on HIV viral load and CD4 cell counts in HIV-infected patients.*", J Acquir Immune Defic Syndr. **2007** Mar 1;44(3):356-9, https://www.ncbi.nlm.nih.gov/pubmed/17159654

However, these experiments on the CD4 cell count and PCR viral load were repeatedly used as evidence of the efficacy of presumed antiviral drugs and thus as evidence of the HIV virus hypothesis.

In addition, parasites can also influence the suspected viral load. Parasites, which are common in Africa, cf.

- Wolday et al. "*Treatment of Intestinal Worms Is Associated With Decreased HIV Plasma Viral Load*", J Acquir Immune Defic Syndr. **2002** Sep 1;31(1):56-62, https://www.ncbi.nlm.nih.gov/pubmed/12352151

"Helminth "load" is correlated to HIV plasma VL, and successful ***deworming is associated with a significant decrease in HIV plasma VL.****"*

How credible, on the other hand, are studies that want to detect a dependence of PCR viral load on skin color?

Cf. also,

- Smith et al. "*Ethnicity and discordance in plasma HIV-1 RNA viral load and CD4+ lymphocyte count in a cohort of HIV-1-infected individuals.*", J Clin Virol. **2003** Jan;26(1):101-7, https://www.ncbi.nlm.nih.gov/pubmed/12589840

"These results suggest that plasma HIV-1 VL is ***discordantly low in Black compared with Caucasian*** *groups stratified for CD4+ count, in this cohort of antiretroviral naive HIV-1-positive individuals living in London."*

The PCR problems also involve considerable difficulties in designing the primers, which (depending on the concentration) can react with each other (*primer dimer*) or even with themselves (*hairpin*). Cf. also

https://www.researchgate.net/post/Any_suggestions_on_why_my_PCR_primers_are_not_working

or

https://www.researchgate.net/post/What_should_I_do_if_the_forward_primer_binds_at_two_sites

or

https://www.researchgate.net/post/How_to_avoid_Primer-Dimer_Formation_and_get_our_gene_amplified

Let's hope that your lab technician has already answered these questions. For further problems with PCR see also Annex II.

13. Stimulation of reverse transcriptase activity and virus structures *in vitro*

It is often overlooked, but hardly a scientific study works with cells freshly taken from the human body. Usually immortalized cell cultures are used. These are cells that were crossed with cancer cells for this purpose. *Immortal* means here that the cells can divide as often as they like. Normal cells lose the cell division capability after about 30 - 50 generations. This is impractical for research. Therefore, there are these immortal cells, which are also commercially available.

If experiments are performed with supposedly HIV+ infected humans, special protocols are used. For *in vitro* experiments on HIV, i.e. experiments that are performed in the test tube, specially ***activated cells*** are used. This means that **PHA** (**phytohaemagglutinin**) and **IL-2** (**interleukin-2**) are added, sometimes other activators, to activate T cells and stimulate the production of putative viruses. The experiments will not work without this activation.

There are so-called standard protocols that have been developed because until the mid 1990s not all laboratories could detect the retroviral activity. Therefore today, most laboratories use so-called standard or consensus protocols for the presumptive detection of the HI virus. The name *standard* does not mean much here. It is not of natural origin. It is only a consensus of the biochemical laboratories according to which ***cooking recipe*** it is the easiest to demonstrate putative retroviral activity, i.e. reverse transcriptase activity.

These often work by the principle of co-culture. That means, there is a second culture of uninfected cell in which the HI virus is meant to be replicated. However, this second culture is **activated** first, so that the replication works.

Cf.

- Montefiori Laboratory Duke University, "*Protocol for HIV-1 Isolation by PBMC Co-Culture*", (January **2014**), https://www.hiv.lanl.gov/content/nab-reference-strains/html/Protocol-for-HIV-1-Isolation-by-PBMC-Co-Culture-January-2014.pdf

*"Primary isolates of HIV-1 are most readily isolated by **mixing PBMC from infected subjects with mitogen-stimulated PBMC from healthy, uninfected donors**. The coculture is incubated in growth medium containing the **T cell growth factor cytokine, IL-2**. Mitogen stimulation of the donor PBMC acts to upregulate the IL-2 receptor, adding to the responsiveness of the cells to exogenously added cytokine."*

Extract from the HIV-1 protocol**:**

„Add PBMC from Infected Subject

1. Thaw a single cryovial of PBMC from each infected subject as described above.

*2. **Transfer the PBMC to a 30 ml culture of PHA-P-stimulated normal donor PBMC in IL2-GM**.*

3. Incubate overnight at 37°C."

One does not activate the cells of an HIV + human directly. But one activates the cells that will be affected by the suspected virus and reproduce it afterwards. See also for the principle,

- Lane, "*Isolation and Expansion of HIV from Cells and Body Fluids by Coculture*", in: Michael N.L., Kim J.H. (eds) HIV Protocols. Methods in Molecular Medicine, vol 17 (**1999**), https://link.springer.com/protocol/10.1385/0-89603-369-4:3 oder

https://www.ncbi.nlm.nih.gov/pubmed/21380650

"*HIV can be recovered from infected patients at all stages of the disease spectrum.* ***Typically, the quantity of biologically active virus, or viral protein, in body tissues is below the level of direct detection by either antigen capture or reverse transcriptase assays****. Consequently, the virus must be expanded in culture. This may be achieved by the* ***cocultivation*** *of patient material with* ***mitogen-stimulated*** *peripheral blood mononuclear cells (PBMCs) from normal, healthy donors. These cocultures are then maintained by regularly scheduled* ***interleukin-2*** *(IL-2) supplemented medium replacement, and the periodic addition of freshly stimulated normal donor PBMCs. During this cocultivation period, culture fluids are harvested at regular intervals and tested for the presence and subsequent replication of HIV. Cultures failing to demonstrate evidence of virus expression within 35 d are usually terminated."*

It has long been known that PHA activates in human cells the production of RNA and DNA and induces reverse transcriptase activity. **This also applies to normal, uninfected cells**, i.e. just those cells in which the suspected HI virus is supposed to multiply.

Note: "*RNA-dependent DNA polymerase " is an old name for the reverse transcriptase enzyme*.

Cf.

- Loeb et al., "*Induction of DNA polymerase in human lymphocytes by phytohemagglutin*n.", Proc Natl Acad Sci U S A. **1968** Nov; 61(3): 827–834, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC305402/

"The lymphocytes of human peripheral blood have been the subject of recent immunologic studies. Although these cells seldom grow or divide in vitro, the addition of phytohemagglutinin (PHA), an extract of the kidney bean (Phaseolus vulgaris), to the culture medium initiates a striking transformation: ***90 per cent of the cells enlarge, synthesize DNA, and divide****."*

- Bobrow et al., "*Stimulated normal human lymphocytes contain a ribonuclease-sensitive DNA polymerase distinct from viral RNA-directed DNA polymerase*.", Proc Natl Acad Sci USA. **1972** Nov;69(11):3228-32, https://www.ncbi.nlm.nih.gov/pubmed/4117771

"Ribonuclease-sensitive DNA synthesis is demonstrated in a cytoplasmic particulate fraction of normal human blood lymphocytes ***stimulated with phytohemagglutinin, but not in unstimulated lymphocytes****."*

- Penner et al., "*RNA-dependent DNA Polymerase in Human Lymphocytes during Gene Activation by Phytohaemagglutinin*", Letters to Editor , Nature New Biology Vol 232, p. 58–61 (14 July **1971**), https://www.nature.com/articles/newbio232058a0

"RNA-DEPENDENT DNA polymerase an activity initially thought to be unique to RNA tumour viruses, is now known to be present in ***normal human lymphocytes****, which are differentiated and seldom divide in vivo or in*

culture. ***The addition of phytohaemagglutinin (PHA) or other mitogens (including appropriate antigens) transforms lymphocytes into actively proliferating cells****."*

- Penner et al., "*RNA-dependent DNA polymerase: presence in normal human cells*.", Biochem Biophys Res Commun. **1971** Mar 19;42(6):1228-34, https://www.ncbi.nlm.nih.gov/pubmed/5550810

"RNA-dependent DNA polymerase has been reported in oncogenic RNA viruses, as well as in human leukemia cells, suggesting a close relationship between this activity and malignancy. ***However, we have detected an RNA-dependent DNA polymerase activity in normal human lymphocytes stimulated with phytohemagglutinin****, indicating either that this enzyme is not unique to RNA-viruses, or that a viral genome is present in non-malignant human cells."*

- Hausen, Stein, "*On the synthesis of RNA in lymphocytes stimulated by phytohemagglutinin. 1. Induction of uridine-kinase and the conversion of uridine to UTP*.", Eur J Biochem. **1968** Apr;4(3):401-6, https://www.ncbi.nlm.nih.gov/pubmed/5690132

„Conversion of uridine to UTP is enhanced in lymphocytes under the influence of phytohemagglutinin concomitant with the induction of uridine kinase. The uridine kinase activity in the induced cells decreases if the cells are treated with antibodies against phytohemagglutinin."

- Bauer, Hofschneider, "*RNA-dependent DNA Polymerase in a "Virus-Free" System*", (**1978**) in Hofschneider P.H., Starlinger P. (eds) Integration and Excision of DNA Molecules. Colloquium der Gesellschaft für Biologische Chemie in Mosbach Baden, Vol 28, https://link.springer.com/chapter/10.1007%2F978-3-642-81203-3_14

„This is a report on the isolation and characterization of an ubiquitously appearing RNA-dependent DNA polymerase from embryonated, ***virus-free chicken eggs****. The enzyme is not the gene product of the polymerase gene of known endogenous or exogenous avian RNA tumor viruses: Its expression is independent of the genetic system of the endogenous avian leukosis virus and seems to be regulated by its own genetic system"*

Retroviral activity is difficult to prove. But without activation, there is no retroviral signal. However, it can be generated with suitable activation in normal cells, too.

I think it's time to give the public a bit more information about these ***HIV cooking recipes*** and make it much more transparent what science actually means by *detecting a virus*.

But the story continues, since it is ***possible to create virus structures by stimulation***, cf.

- Bauer et al., "RNA-dependent DNA polymerase (reverse transcriptase).", Blut. **1977** Jul 20;35(1):3-9, https://www.ncbi.nlm.nih.gov/pubmed/70251

"Examples for DNA-dependent DNA polymerase synthesis with an RNA primer are the activities from stimulated lymphocytes [7] ***and from particles which can be found in the culture medium of normal human***

fibroblasts *[15]. The latter activity is of special interest: These particles show several properties which usually are believed to be characteristic for RNA tumour viruses."*

You might wonder: ***Particles***? What ***particles***?

Cf. also

- Margalith et al., "*Studies on the DNA polymerase activity contained in particles released from human embryo cell monolayers*.", Biochim Biophys Acta. **1976** Mar 17;425(3):305-15, https://www.ncbi.nlm.nih.gov/pubmed/1259973

- Gerard et al., "*Detection of reverse transcriptase in human breast tumours with poly(Cm)-oligo(dG).*", Nature. **1975** Jul 10;256(5513):140-3, https://www.ncbi.nlm.nih.gov/pubmed/50561

*"**PARTICLES** having the density of type-C RNA tumour viruses, possessing reverse transcriptase (RNA-directed DNA polymerase) activity, and containing high molecular weight RNA that shares a portion of its base sequences with the RNA of murine RNA tumour viruses, have been reported to be present in several types of human malignant tissues, but not in their normal counterparts (review, see ref. 1)"*

- Watrach, „*Induction of oncornavirus-like particles in cell line of canine mammary carcinoma*.", Br J Cancer. **1978** Nov;38(5):639-42, https://www.ncbi.nlm.nih.gov/pubmed/728353

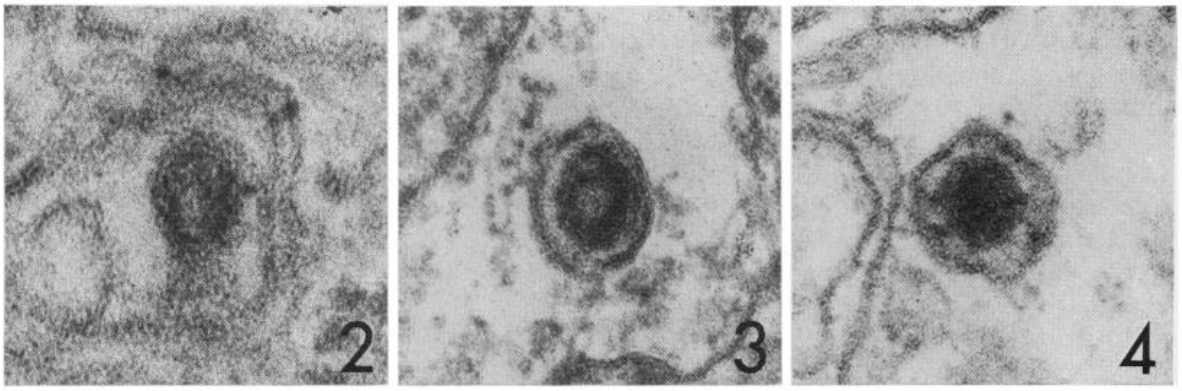


FIG. 2.—Virus-like particle budding in cytoplasmic cisterna of CMT-14B cell. × 150,000.
FIG. 3.—Mature virus-like particle with dense, ring-like, centrally placed nucleoid in cytoplasmic vacuole. × 140,000.
FIG. 4.—Mature virus-like particle with dense nucleoid in intercellular space. × 140,000.

"Examination of the sectioned pellet obtained from the supernatant fluid of treated cultures revealed the presence of a small number of oncornavirus-like particles ranging in diameter from 100 to 130 nm. Their outer membrane had a typical bilaminar structure and was 7 to 8 nm thick. The nucleoid, measuring 50 to 75 nm, was condensed and concentrically placed. No virus particles were detected in control culture fluid or cells."

*"These studies tend to indicate that CMT-14B virus-like particles may represent an **endogenous oncornavirus chemically activated in CMT-14B cell cultures**. This observation is supported by the negative results obtained from untreated cultures. Consequently, the possibility of contamination of cultures by an unrelated oncornavirus, e.g., from serum in the culture medium, can be discounted."*

It is legitimate to ask about the contributions of induced viral structures and how to discriminate against them, e.g. in diagnosis. On the other hand, it can be ruled out that electron microscopic (EM) images were taken of every HIV+ measured person. Otherwise, the same pictures would not be shown for 30 years.

Attention: the discussion about the detection of a virus must be separated from the discussion about a pathogenic virus. That means, the detection of a virus does not mean that you have found a pathogen. There are enough harmless viruses. On the other hand, the question should be answered why anti-body against the putative HIV virus serve for diagnosis, but at the same time do not immunize. ***The HI virus is the only virus with this property***.

For virus particles in activated cell cultures cf. also

- de Harven, "*Human Endogenous Retroviruses and AIDS Research: Confusion, Consensus, or Science?*", J. Am. Phys. Surg. Vol 15 (3), **2010**, http://www.jpands.org/vol15no3/deharven.pdf

"All the images of particles supposedly representing HIV and published in scientific as well as in lay publications derive from EM studies of cell cultures. ***They never show HIV particles coming directly from an AIDS patient.****"*

"Cord blood lymphocytes are placenta-derived cells. The human placenta is well known for its high content of HERVs, with EM-recognizable retrovirus particles."

"The EM observation of typical retroviral particles in the 1983 Pasteur paper can alternatively be explained by the presence of placenta-derived, Polybrene-activated HERVs. ***However, this EM observation does not support the existence of an AIDS-related, exogenous retrovirus****. Obviously, confounding by HERVs cannot be ignored in the objective analysis of clinical as well as basic HIV/AIDS research."*

"*Secondly, in the general classification of animal virology,* ***very large numbers of viruses are nonpathogenic****, as was well illustrated in the 1960s in a special conference, at the New York Academy of Sciences, under the title "****Viruses in Search of Diseases****." Obviously, all nonpathogenic (i.e. "harmless") viruses are clearly visible under the EM.* ***Pathogenic and nonpathogenic viruses look identical under the EM****. In AIDS research,* ***retroviral particles were observed by EM only in complex cell culture systems, never directly in the plasma, nor in the tissues of any AIDS patient****."*

- Strand et al., "*Type-C RNA virus gene expression in human tissue*.", J Virol. **1974** Dec;14(6):1584-96, https://www.ncbi.nlm.nih.gov/pubmed/4372412

"*A hypothesis suggested by these data is that* ***many, if not all, humans harbor at least part of the genome of one or more type-C viruses****, the properties of which are similar to those of viruses from other mammalian species, particularly primates."*

Comment: "*Type C RNA viruses are a distinct class of vertebrate viruses which share a common morphology, protein composition, and viral life cycle, have single-stranded RNA as their viral genome, and contain an RNA-directed DNA polymerase (****reverse transcriptase****)."*

Cf. Lieber, Todaro, "*Mammalian Type C RNA Viruses*", (**1975**) In: Becker F.F. (eds) Cancer a Comprehensive Treatise 2. Cancer, Vol 2, https://link.springer.com/chapter/10.1007/978-1-4684-2733-2_3

Thus, more than 10 years before the announcement of the HIV virus as the putative cause of AIDS, it was clear that by appropriate stimulation and activation, reverse transcriptase activity as well as viral structures could be induced in cells. Presumably, this is also the reason why there was so long and intensive research on **RNA viruses as the cause of cancer**.

These expectations did not fulfill cf.

- Duesberg, „*Retroviruses as carcinogens and pathogens: expectations and reality*.", Cancer Res. **1987** Mar 1;47(5):1199-220, https://www.ncbi.nlm.nih.gov/pubmed/3028606

und

- Duesberg, Schwartz, "*Latent viruses and mutated oncogenes: no evidence for pathogenicity*.", Prog Nucleic Acid Res Mol Biol. **1992**;43:135-204, https://www.ncbi.nlm.nih.gov/pubmed/1410445

(**Do not forget:** Dr. Duesberg is allowed to say something about ***cancer*** according to Scientific American!)

Yes, there seems to be a connection between cell stress, e.g. by cancer, and reverse transcriptase activity and virus structures, at least in suitably activated or stimulated cells. However, it is open whether one has not created the cause for this in the experiments itself.

14. CD4 cell count - therapy control in the last 25 years

The problems of PCR and the deficits of the diagnosis especially in the determination of the presumed viral load have been discussed above. The second "*pillar*" on which the current HIV therapy control is placed concerns the measurement of the CD4 cell count (see also the HIV book by Hoffmann and Rockstroh). These are cells of the human immune system whose number is being counted and the decline of which is supposed to indicate the progression of a disease. Unfortunately, that is not true, cf.

- Rodriguez et al. „*Predictive Value of Plasma HIV RNA Level on Rate of CD4 T-Cell Decline in Untreated HIV Infection*", JAMA, Sep 27, **2006,** Vol 296 (12), https://www.ncbi.nlm.nih.gov/pubmed/17003398

If it is as the authors write that "***only a small proportion of CD4 cell loss variability (4% -6%) could be explained by presenting plasma HIV RNA level***", then this would be a very questionable tool.

Cf. also

- Henry et al. „*Explaining, predicting, and treating HIV-associated CD4 cell loss: after 25 years still a puzzle.*", JAMA, Sep 27, **2006,** 296(12), p. 1523-5, https://www.ncbi.nlm.nih.gov/pubmed/17003402

- Ying et al., „*CD4 Cell Count: Declining Value for Antiretroviral Therapy Eligibility*", Clin. Inf. Dis. **2016**; 62(8):1022–8, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5006297/

„*Studies suggest that **CD4 counts early in HIV infection do not predict relevant public health outcomes** such as disease progression, mortality, and HIV transmission in people living with HIV. **CD4 counts also vary widely within individuals and among populations, leading to imprecise measurements and arbitrary ART initiation***."

"*Consequently, CD4 measurements indicate neither one's prognosis nor when retesting should occur, […]".*

*"CONCLUSIONS: Historically, there has been discordance in global ART initiation guidelines based on CD4 counts, **suggesting that CD4 counts may not be a reliable surrogate marker for ART initiation**. They do not predict disease progression or transmission, produce widely varying results within and among populations, and **pose a barrier to scaling up HIV care and decentralization**."*

This coincides with the information provided by the WHO.

- Doherty, "*WHO guidelines on the use of CD4, Viral Load and EID tests for initiation and monitoring of ART*", **2015** http://www.who.int/hiv/amds/102_WHO_Guidelines_on_CD4_and_VL_for_ART_Doherty.pdf (Slide 13):

"*In settings where both CD4 and viral load are available, countries **could consider reducing or eliminating CD4 for monitoring.**"*

- Gazzola et al., "*The absence of CD4+ T cell count recovery despite receipt of virologically suppressive highly active antiretroviral therapy: clinical risk, immunological gaps, and therapeutic options*.", Clin Infect Dis. **2009** Feb 1;48(3):328-37, https://www.ncbi.nlm.nih.gov/pubmed/19123868

"Up to 30% of human immunodeficiency virus (HIV)-infected patients who are receiving long-term highly active antiretroviral therapy do not exhibit a marked increase in the CD4(+) T cell count, ***despite achieving complete suppression of the HIV load."***

- Moore et al. "*CD4+ T-cell count monitoring does not accurately identify HIV-infected adults with virologic failure receiving antiretroviral therapy*.", J Acquir Immune Defic Syndr. **2008** Dec 15;49(5):477-84, https://www.ncbi.nlm.nih.gov/pubmed/18989232

"***CD4 cell count monitoring does not accurately identify individuals with virologic failure among patients taking ART.***"

That's all a bit arbitrary. What was the standard for the last 25 years? And what is expected of women and children? They are not even near the original AIDS population in the early 80s in San Francisco.

And how does that affect the statistics, e.g. of the Robert Koch Institute (RKI)? For example,

- Epidemiologisches Bulletin Nr. 47, 23. November **2017**, https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2017/Ausgaben/47_17.pdf?__blob=publicationFile

*„Auch die Anteile der HIV-Diagnosen bei fortgeschrittenen Immundefekt (****AIDS oder ein CD4-Wert < 200 Zellen/µl Blut****) verlaufen konstant und betreffen etwa 30 % der HIV-Diagnosen bei MSM und IVD und etwa 35 % der HIV-Diagnosen bei Heterosexuellen."*

Translation:
*„The proportion of HIV diagnoses in advanced immunodeficiency syndrome (****AIDS or CD4 <200 cells / µl blood****) is also constant, accounting for about 30% of HIV diagnoses in MSM and IVD and about 35% of HIV diagnoses in heterosexuals."*

AIDS is defined by the CD4 cell count. It seems there is not even a standard, what is the normal amount of CD4 cells, cf.

- Crampin, „*Normal Range of CD4 Cell Counts and Temporal Changes in Two HIV Negative Malawian Populations*", The Open AIDS Journal, **2011**, 5, 74-79, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3162193/

"*1.5% and 6% respectively had baseline counts below 350 cells/µl and 1.5% and* ***2.5% below 250 cells per µl****.* ***Transient dips to below 250 cells/µl were observed in seven individuals, with two individuals having persistently low CD4 counts over more than one year."***

„In common with neighbouring countries, ***HIV-negative populations in Malawi have CD4 counts considerably lower than European reference ranges, and healthy individuals may have persistently or transiently low counts.*** *Within Malawi, ranges differ according to the selected population."*

„[…] but ***given the investment in CD4 infrastructure****, it is important to ensure that its usefulness is optimised locally."*

250 cells and less per µl for 1 year would have been AIDS in HIV + people. That would have meant HAART with all the side effects. A newborn would not even have had a say.

Let us ask the German AIDS Society how it sees the whole thing, cf.

- DAIG, „*Deutsch-Österreichische Leitlinien zur antiretroviralen Therapie der HIV-1-Infektion*“, Version 8 auf der Basis der Konsensuskonferenz vom 10.4.**2019,** https://daignet.de/site-content/hiv-therapie/leitlinien-1

*„**Bei allen Patienten mit weniger als 500 CD4-Zellen/µL soll eine Therapie erfolgen**. Die Dringlichkeit des Therapiebeginns (binnen Tagen, Wochen oder Monaten) erhöht sich in Abhängigkeit von der CD4+-Zellzahl: Je niedriger die CD4+-Zellzahl, desto dringlicher die Therapie. Bei weniger als 200 CD4+-Zellen steigt das Risiko opportunistischer Folgeerkrankungen erheblich, und Morbidität und Mortalität bleiben trotz erfolgreicher Therapie erhöht (22), der Behandlungsbeginn ist daher dringlich. Bei Vorliegen bestimmter opportunistischer Infektionen sollte die ART wegen des Risikos eines **Immunrekonstitutionssyndroms** verzögert begonnen werden. Diesbezüglich wird auf die DAIG-Leitlinie Opportunistische Infektionen verwiesen.“*

[Translation: *German-Austrian guidelines for antiretroviral therapy of HIV-1 infection*]

*“**All patients with less than 500 CD4 cells/µL should receive treatment**. The urgency of starting therapy (days, weeks or months) increases depending on the CD4 cell count: the lower the CD4 cell count, the more urgent the therapy. In fewer than 200 CD4 cells, the risk of opportunistic sequelae increases significantly, and morbidity and mortality remain elevated despite successful therapy (22), and therefore treatment is urgent. In the presence of certain opportunistic infections, ART should be delayed due to the risk of the **immune reconstitution inflammatory syndrome**. In this regard, reference is made to the DAIG guideline Opportunistic Infections.”*

The subject that classical infections, which are very common in risk groups, additionally influence the measurements, has already been discussed above. In fact, classical infections as well as parasites affect the so-called viral load and the CD4 cell counts, cf.

- Buchacz et al, “*Syphilis increases HIV viral load and decreases CD4 cell count*”, AIDS **2004**, 18:2075–2079, https://www.ncbi.nlm.nih.gov/pubmed/15577629

- Palacios et al., „*Impact of syphilis infection on HIV viral load and CD4 cell counts in HIV-infected patients.*”, J Acquir Immune Defic Syndr. **2007** Mar 1;44(3):356-9, https://www.ncbi.nlm.nih.gov/pubmed/17159654

- Mesiha et al., “*False Positive HIV Result and Low CD4 in Babesiosis*.”, Ann Clin Lab Sci. **2017** Aug;47(4):516-517, https://www.ncbi.nlm.nih.gov/pubmed/28801382

However, these experiments on the CD4 cell count and PCR viral load were repeatedly used as evidence of the efficacy of presumed antiviral drugs and thus as evidence of the HIV virus hypothesis.

And what exactly is a therapy control under HAART based on the CD4 cell count worth?

14.1. CD4 cell count in HIV-negative tuberculosis patients

It is often said that there is a special link between HIV and tuberculosis and that they are a deadly duo. It is overlooked that **tuberculosis is AIDS-defining**, cf.

- "*Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS among Adolescents and Adults*", **1993**, http://www.who.int/hiv/strategic/en/cdc_1993_hivaids_def.pdf

"*This expansion includes the addition of three clinical conditions*

- ***pulmonary tuberculosis**, recurrent pneumonia, and **invasive cervical cancer** -- and retains the 23 clinical conditions in the AIDS surveillance case definition published in 1987 (2); **it is to be used by all states for AIDS case reporting effective January 1, 1993**."*

Likewise from the

- *European AIDS Case Definition for Children*, **1995**, http://www.who.int/hiv/strategic/en/euro_1995_Def.pdf

page 47:

*"Regardless of the presence of other causes of immunodeficiency (I.A), in the presence of laboratory evidence for HIV infection (Annex 1 -paragraph A), any disease listed above (I.B) or below (II.A or II.B) **indicates a diagnosis of AIDS**.*

8. Mycobacterium tuberculosis, disseminated or extrapulmonary"

page 50:

*"Annex 2. Definitive Diagnostic Methods for Dieases **Indicative of AIDS in Children**:*

tuberculosis other mycobacteriosis salmonellosis other bacterial infection"

Also cf.

- HIV-Infektion/AIDS - RKI-Ratgeber, Stand: 08.03.**2016**, https://www.rki.de/DE/Content/Infekt/EpidBull/Merkblaetter/Ratgeber_HIV_AIDS.html

*„Eine weitere bedeutende **AIDS-definierende Erkrankung** ist die aktive Tuberkulose. Diese ist i.e.S. keine opportunistische Infektion, da ein Erregernachweis von Mycobacterium tuberculosis auch bei immunkompetenten Personen bedeutet, dass eine aktive Tuberkulose vorliegt.*"

Translation

*„ Another major **AIDS-defining disease is active tuberculosis**. This is in the narrower sense no opportunistic infection, since detecting pathogens of Mycobacterium tuberculosis also means that there is active tuberculosis even in immunocompetent individuals."*

According to the same definitions of AIDS, prolonged fever or diarrhea or weight loss are AIDS-defining, as a kind of catchall element or in regions where there is no laboratory infrastructure.

- "*Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults*", **1993**, http://www.who.int/hiv/strategic/en/cdc_1993_hivaids_def.pdf

"*Constitutional symptoms, such as fever (38.5 C) or diarrhea lasting greater than 1 month.*"

Tuberculosis is a very serious disease that has been around for a long time, long before AIDS. However, uncomplicated tuberculosis usually has a good prognosis.

Now HIV+ measured tuberculosis patients have two diagnoses, tuberculosis and HIV +, and according to the definition, he / she has AIDS.

The supposed evidence for immunosuppression (weakening of the immune system) by the putative HI virus is a reduction in the CD4 cell count, see above. And at low CD4 cell counts, doctors should start with HAART according to the professional rules.

However, what if the AIDS-defining disease, tuberculosis, also lowers the CD4 cell count in the HIV-negative patients?

That is exactly the case, cf.

- Skogmar et al., "*CD4 Cell Levels during Treatment for Tuberculosis (TB) in Ethiopian Adults and Clinical Markers Associated with CD4 Lymphocytopenia*", PLoS One. **2013**; 8(12): e83270, https://www.ncbi.nlm.nih.gov/pubmed/24358268

*"In total, 1116 TB patients were included (307 HIV-infected). Among **809 HIV-negative patients, 200 (25%) had subnormal CD4 cell counts** (<500 cells/mm(3)), with <350 cells/mm(3) in 82 (10%) individuals. **CD4 cell levels increased significantly during the course of ATT in both HIV+ and HIV- TB-patients**, but did not reach the levels in healthy subjects"*

HAART would start with these people, with catastrophic consequences for the immune system and the prognosis of the healing process.

Also, the recovery of CD4 cell count after anti-tuberculosis treatment in HIV-negative people shows that tuberculosis affects this bio-marker.

- Luo et al., "*Immunological recovery in patients with pulmonary tuberculosis after intensive phase treatment*", J Int Med Res. **2018** Sep; 46(9): 3539–3551, https://www.ncbi.nlm.nih.gov/pubmed/29756540

"Inclusion criteria were as follows: …

*(4) **seronegative** for human immunodeficiency virus (HIV)"*

"After 2 months of intensive phase anti-TB treatment, a reduction in the percentage of CD4+ T cells showed a significant restoration similar to that of controls."

These facts have been known for a long time, cf.

- Jones et al., "*CD4 cell counts in human immunodeficiency virus-negative patients with tuberculosis*.", Clin Infect Dis. **1997** May;24(5):988-91, https://www.ncbi.nlm.nih.gov/pubmed/9142808

"*We evaluated 85 human immunodeficiency virus **(HIV)-negative patients** with tuberculosis for clinical features and CD4 cell counts. Thirty-seven patients had low CD4 cell counts (mean +/- SD, 341 +/- 116 cells/microL), and 48 patients had normal CD4 cell counts (mean +/- SD, 830 +/- 254 cells/microL).*"

"*The CD4 cell counts returned to normal levels in most patients after 1 month of therapy.*"

*"We confirmed previous studies demonstrating that **CD4 cell counts are depressed in HIV-negative patients with tuberculosis**"*

However, no one discriminates in a HIV + measured tuberculosis patient against the CD4 cell loss by the tuberculosis. This is simply attributed to the acquired immunodeficiency. However, at a CD4 cell count <500 cells per µl, the German AIDS Society recommends the immediate onset of HAART in HIV+ measured people, see above:

*„**Bei allen Patienten mit weniger als 500 CD4-Zellen/µL soll eine Therapie erfolgen**"*

Translation:

*„**All patients with less than 500 CD4 cells / µL should receive treatment**.*

- Pilheu et al., "*CD4+ T-lymphocytopenia in severe pulmonary tuberculosis without evidence of human immunodeficiency virus infection*.", Int J Tuberc Lung Dis. **1997** Oct;1(5):422-6, https://www.ncbi.nlm.nih.gov/pubmed/9441096

"*Based on the findings of this study, we feel that it is of value to measure the CD4 and CD8 T-lymphocyte counts in STP patients with a compromised general condition and with significant weight loss at the beginning of treatment. **Those patients with a CD4 count of < 300/mm3 have a very poor prognosis** and, in addition to the regular antituberculosis drugs, will require intensive care during the first weeks of treatment."*

- Gao et al., "*Characterization of CD4/CD8+ αβ and Vγ2Vδ2+ T cells in **HIV-negative individuals** with different Mycobacterium tuberculosis infection statuses*.", Hum Immunol. **2015** Nov;76(11):801-7, https://www.ncbi.nlm.nih.gov/pubmed/26429305

*„The absolute numbers of T cell subsets, including CD3+ **CD4+**, CD3+ CD8+ αβ and Vγ2Vδ2+ T cells, were **significantly reduced in active tuberculosis** compared with latent tuberculosis or the healthy controls. "*

- Ollé-Goig et al., "*Profound reduction of CD4+ lymphocytes without HIV infection: two cases from the horn of Africa*.", Afr Health Sci. **2012** Sep;12(3):331-3, https://www.ncbi.nlm.nih.gov/pubmed/23382748

*"We report two HIV-negative patients with idiopathic CD4+ lymphocytopenia and AIDS-defining events diagnosed in Djibouti. The first patient developed lesions of Kaposi's sarcoma and the second one presented with **pulmonary tuberculosis**. Both patients died with severe immunodepression. In poor resource-areas*

where HIV testing may not be available it is important to bear in mind that ***severe immunodepression and a clinical presentation compatible with AIDS do not necessary carry the diagnosis of AIDS****."*

- Zaharatos et al., "*Profound T-lymphocytopenia and cryptococcemia in a human immunodeficiency virus-****seronegative patient*** *with disseminated tuberculosis*.", Clin Infect Dis. **2001** Dec 1;33(11):E125-8, https://www.ncbi.nlm.nih.gov/pubmed/11692315

"A 47-year-old human immunodeficiency virus-seronegative West African man who presented in extremis with cachexia, lymphadenopathy, multiple organ dysfunction, and marked T-lymphocytopenia received the diagnosis of disseminated tuberculosis, cryptococcal pneumonia, and cryptococcemia. His subsequent course and our review of the literature suggest that the profound T-lymphocytopenia and ensuing cryptococcal disease were likely attributable to ***disseminated tuberculosis****."*

- Mhmoud et al., "*CD4+ T-lymphocytopenia in HIV-negative tuberculosis patients in Sudan*.", J Infect. **2012** Oct;65(4):370-2, https://www.ncbi.nlm.nih.gov/pubmed/22728173

- Al-Aska et al., "*CD4+ T-lymphopenia in HIV negative tuberculous patients at King Khalid University Hospital in Riyadh, Saudi Arabia*.", Eur J Med Res. **2011** Jun 21;16(6):285-8, https://www.ncbi.nlm.nih.gov/pubmed/21810564

"We conclude that tuberculosis may be associated with CD4 and CD8 lymphopenia ***even in patients without human immunodeficiency virus infection****, there was the tendency of recovery towards normality especially of the CD4 and CD8 counts after treatment, and that disseminated disease is associated specifically with profound CD4 lymphopenia."*

- Uppal et al., "*Comparison of CD4 and CD8 lymphocyte counts in HIV-negative pulmonary TB patients with those in normal blood donors and the effect of antitubercular treatment: hospital-based flow cytometric study*.", Cytometry B Clin Cytom. **2004** Sep;61(1):20-6, https://www.ncbi.nlm.nih.gov/pubmed/15351978

*"****CD4 counts and percentages of CD4 were significantly lower,*** *but CD8 values were normal, in patients with pulmonary TB when compared with values obtained in normal blood donors. The CD4/CD8 ratio was significantly lower in patients with TB.* ***The CD4 counts normalized with antitubercular treatment.****"*

- Atomsa et al., "*Immunological markers and hematological parameters among newly diagnosed tuberculosis patients at Jimma University Specialized Hospital*.", Ethiop J Health Sci. **2014** Oct;24(4):311-8, https://www.ncbi.nlm.nih.gov/pubmed/25489195

"Newly diagnosed TB patients who have already started anti-TB treatment, receiving any kind of immunosuppressive drugs, known or suspected history of other chronic disease, pregnant women and ***HIV positive individuals were excluded****."*

"*Analysis of variance revealed that mean ± SD of CD4 count of male TB patients (650 ± 224cells/µl) was* ***significantly lower*** *than male control group (883 ± 256 cells/µl). In a similar manner, the mean CD4 count of female TB patients (793 ± 332cells/µl) was* ***lower than female control group*** *(975 ± 300 cells/µl)"*

"CD4 lymphopenia was significant among TB patients."

The CD4 cell count also varies with the season:

- Gomo et al., "*Predictors and reference values of CD4 and CD8 T lymphocyte counts in pregnancy: a cross sectional study among **HIV negative women** in Zimbabwe*.", Cent Afr J Med. **2004** Jan-Feb;50(1-2):10-9, https://www.ncbi.nlm.nih.gov/pubmed/15490719

"The late rainy season was associated with higher CD4 counts…"

*"Gestational age, gravidity, micronutrient status and **season** influence T lymphocyte subset levels and need to be considered when designing clinical management and intervention strategies for pregnant women. The data underscores the need for **local** reference values."*

These experimental findings also leave the bystander cell problem (see below, only 5% of CD4 cells are infected with HIV, the not infected cells die and at the same time there is a high daily turnover of these cells) in a different light. How should the CD4 cell count be reduced by HIV? It seems what is really measured here are the effects of the other infections in addition to the broad and strongly varying distribution of the CD4 cell count in the total population.

When we talk about HIV+, we almost always talk about drug abuse and classical infections (see also Appendix III). Partially, co-infections are AIDS-defining, e.g. tuberculosis. However, both drugs and classical infections have an immunosuppressive effect on the bio-marker, CD4 cell count (for drugs see also below).

It can be assumed that the pressure on HIV+ measured people, together with presumably significant sleep deprivation or poor sleep, also influences this bio-marker. Especially, if the person suffers from a *classical infection*.

I wonder, what does the definition of AIDS by bio-markers and existing diseases mean for statistics, e.g. in Africa. Is not all that ***a little too comfortable***?

14.2. Other causes of low CD4 cell count in HIV-negative people

Aside from the fact that nobody knows what the standard of the CD4 cell count is in a healthy person, see above, it has long been known that there can be many causes for a low cell count. This is the case for people who are otherwise ill, or under great stress.

But even a slight sunburn may be sufficient to lower the CD4 cell count, cf.

- Hersey et al. "*Immunological effects of solarium exposure*.", Lancet. **1983** Mar 1 2;1(8324):545-8, https://www.ncbi.nlm.nih.gov/pubmed/6131254

"*OKT4+ helper T cells were reduced and there was a significant decrease in the OKT4/OKT8 ratio*."

- Hersey et al., "*Alteration of T cell subsets and induction of suppressor T cell activity in normal subjects after exposure to sunlight*.", J Immunol. **1983** Jul;131(1):171-4, https://www.ncbi.nlm.nih.gov/pubmed/6223071

"*In comparison to concurrent studies on 13 age- and sex-matched controls, sun-exposed subjects had a significant increase in their circulation of T cells recognized by OKT8 monoclonal antibodies and a **decrease in OKT4 positive T cells***."

Nutrition also plays a role.

- Chandra, "*Nutrition and the immune system: an introduction*.", Am J Clin Nutr. **1997** Aug;66(2):460S-463S, https://www.ncbi.nlm.nih.gov/pubmed/9250133

"*Figure3. There is a marked reduction in the proportion of CD4+ helper inducer cells in **malnourished children** (…).*"

In malaria disease (frequent in Africa), the CD4 cell number of malaria-ill HIV- persons may be lower than in HIV+ persons, cf.

- Chirenda, "*Low CD4 count in HIV negative malaria cases and normal CD4 count in HIV positive and malaria negative patients*.", Cent Afr J Med. **1999** Sep;45(9):248, https://www.ncbi.nlm.nih.gov/pubmed/11019476

The behaviour of the mother during pregnancy also plays a role. The children of drug-addicted mothers have lower CD4 cell counts than children of healthy mothers, regardless of HIV.

- Culver, "*Lymphocyte abnormalities in infants born to drug-abusing mothers*", J. Ped. August **1987**, Vol 111 (2), p. 230–235, https://www.jpeds.com/article/S0022-3476(87)80073-2/pdf

"*The OKT4/OKT8 ratio decreased with age in the drug-exposed infants compared with control infants (P<0.005). There was no evidence of CMV infection in either group. One mother and her infant had antibody to HIV. Our data demonstrate that infants of intravenous drug-using mothers have distinct immunologic differences at birth compared with nondrug-exposed infants and that these persist throughout the first year of life. **The cause appears unrelated to intrauterine viral infection, suggesting a direct toxic effect of the drugs on fetal immunologic development***."

It seems that almost every disease lowers the CD4 cell count, cf.

- Kavuma Mwanje et al., "*Association between CD4 T cell counts and the immune status among adult **critically ill HIV-negative patients** in intensive care units in Uganda*.", AAS Open Res. **2019** Jan 8;2:2, https://www.ncbi.nlm.nih.gov/pubmed/31517248

*"CD4 T cell counts were generally low among **HIV-negative critically ill patients**. Low CD4 T cells did not predict ICU mortality at day 28."*

"After a 28-day follow up, ***71*** *[****54.6%,*** *95% CI (45.9-63.3)] were found to have* ***CD4 counts less than 500 cells/mm³****, […]"*

In ***71 persons***, or ***54%*** of the examined group, in Kavuma Mwanje *et al.* (2019) antiretroviral therapy should start, if they were measured HIV+, according to current standards - with all the severe side effects/co-morbidities listed above.

It has been known for at least 24 years that the CD4 cell count, ***the AIDS criterion***, is useless, cf.

- Feeney et al., "*T-lymphocyte subsets in acute illness*.", Crit Care Med. **1995** Oct;23(10):1680-5, https://www.ncbi.nlm.nih.gov/pubmed/7587233

"Despite only three (2.9%) of 102 patients testing positive for HIV antibodies, 41% (42/102) of patients had CD4 concentrations of < 400 cells/microL, and 29% (29/102) had CD4 concentrations of < 300 cells/microL"

"*Acute illness alone,* ***in the absence of HIV infection****, can be associated with profound decreases of T-lymphocyte populations. This problem is unpredictable and does not correlate with severity of illness, predicted mortality rate, or actual mortality rate*. ***No conclusions regarding HIV serostatus or survival can be made based on single measurements of T-cell concentrations in acutely ill hospitalized patients.***"

- Williams et al., "*Alterations in lymphocyte cell surface markers during various human infections*", Am. J. Med. November **1983** Vol 75 (5), p. 807–816, https://www.amjmed.com/article/0002-9343(83)90412-6/abstract

"***Significant depression was recorded in total numbers of T cells*** *and T cell helper-inducer and suppressor-cytotoxic subsets in pneumonia, acute pyelonephritis, and severe generalized sepsis*."

Stress also negatively affects the CD4 cell count, cf.

- Herbert, Cohen, "*Stress and immunity in humans: a meta-analytic review*.", Psychosom Med. **1993** Jul-Aug;55(4):364-79, https://www.ncbi.nlm.nih.gov/pubmed/8416086

„*In addition,* ***stress is negatively related*** *to the number of circulating B cells (-.243), T cells (-.256), helper T cells (-.204), suppressor/cytotoxic T cells (-.387), and large granular lymphocytes (-.319;…*"

- Kennedy, "*Immunological consequences of acute and chronic stressors: mediating role of interpersonal relationships*.", Br J Med Psychol. **1988** Mar;61 (Pt 1):77-85, https://www.ncbi.nlm.nih.gov/pubmed/3282539

„*Immune changes included both quantitative and qualitative changes in immune cells, including changes in herpes virus latency,* ***decreases in the percentages of T-helper lymphocytes*** *and decreases in the numbers and function of natural killer cells. These effects occurred independently of changes in nutrition.* ***Psychological variables, including loneliness, attachment and depression were related to the immune changes***."

And who wants to claim that HIV+ people are not under stress? However, this stress affects the bio-marker, which is supposed to predict the "*disease*".

Drug abuse lowers the CD4 cell count and this is very common in risk groups, see also below.

- McDonough, „*Alteration of T and null lymphocyte frequencies in the peripheral blood of human opiate addicts: in vivo evidence for opiate receptor sites on T lymphocytes*.", J Immunol. **1980** Dec;125(6):2539-43, https://www.ncbi.nlm.nih.gov/pubmed/6253568

"*These results support the hypothesis that **opiates can alter T lymphocyte number** and function in vivo, and that this alteration may **produce a significant degeneration in the immune competence** of street opiate addicts.*"

It is completely incomprehensible how, despite this data material, one could use the CD4 cell number, especially in risk groups with numerous classical infections and drug abuse or in Africa, as a bio-marker for the **definition of AIDS** and for therapy control.

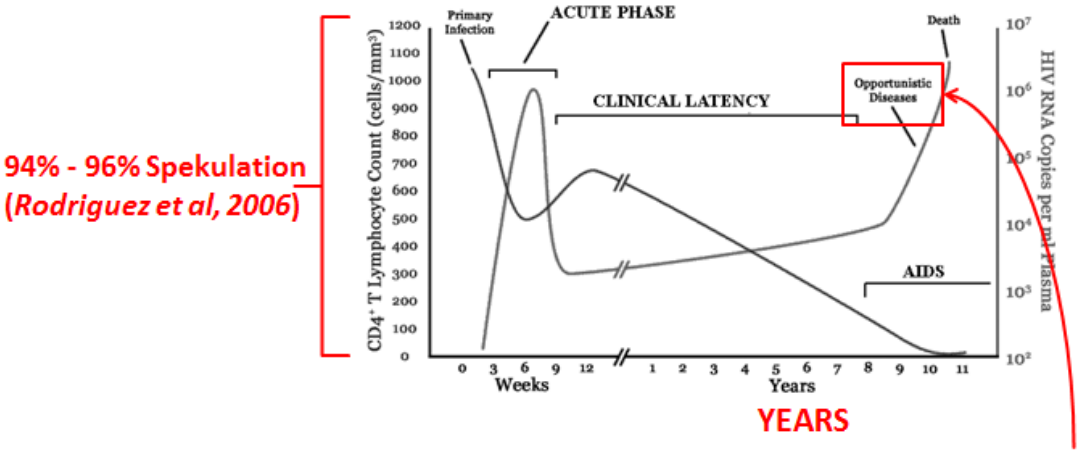
15. HIV / AIDS statistics

It has already been mentioned above, AIDS is a catalog disease, cf. WHO, „*Overview of Internationally Used HIV/AIDS Case Definitions*“, http://www.who.int/hiv/strategic/surveillance/definitions/en/

That means that there are no specific clinical symptoms, such as in case of chickenpox or influenza, which occur promptly after the infection. This timely response to a pathogen is a direct consequence of the multiplication of pathogens in the body, which occurs exponentially in the cell division rhythm, until the immune system responds and the body fights the pathogen. Anyone who has had a flu knows that one does not overlook it.

Unlike the "*slow virus*" (*lenti virus*). Here, there are latencies of 10 years and more, without any clinical symptom. Only in the opportunistic infection, which corresponds to a long-known disease, the effect of the suspected HI virus would show.

It should be noted that in high risk groups classical infections by classical pathogens occur frequently, e.g. syphilis, HBV or herpes (genital warts), see Annex III. These infections are independent of HIV and do not say anything about a person's immune status. They are an indication of a risky behavior, e.g. through unprotected anal intercourse. They are strictly to be distinguished from "*opportunistic infections*" due to an untreated immune deficiency caused by whatever, e.g. drug abuse. In case of HIV it is said that years can pass before they occur. During this time, the human will show no symptoms, except for the side effects of HAART, especially in non-risk groups, without classical infections and / or drugs.



- In Nicht-Risikogruppen nach ca. 8 Jahren HAART (siehe unten) von opportunistischen Infektionen zu sprechen wäre eine ***self-fullfilling prophecy.***

Translation:

*“To speak of opportunistic infections after 8 years of HAART in non-risk groups would be a **self-fulfilling prophecy**.”*

However, it is not always diseases with a specific clinical picture that are used for diagnosis (defining AIDS). Fever lasting for 1 month or diarrhea is sufficient for an AIDS diagnosis, cf.

- "*Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS among Adolescents and Adults*", **1993**, http://www.who.int/hiv/strategic/en/cdc_1993_hivaids_def.pdf (page 3)

„*Constitutional symptoms, such as fever (38.5 C) or diarrhea lasting greater than 1 month*"

This is probably very convenient for developing countries and probably played a significant role in the early years of AIDS statistics.

Likewise, weight loss is AIDS defining, ibid,

„*HIV wasting syndrome* ***Findings of profound involuntary weight loss of greater than 10% of baseline body weight*** *plus either chronic diarrhea (at least two loose stools per day for greater than or equal to 30 days), or chronic weakness and documented fever (for greater than or equal to 30 days, intermittent or constant) in the absence of a concurrent illness or condition other than HIV infection that could explain the findings (e.g., cancer, tuberculosis, cryptosporidiosis, or other specific enteritis).*"

How should someone keep his weight if he or she has to vomit permanently due to the strong cell toxins of HAART therapy, see above?

At the same time, one can state that if someone has tuberculosis and is HIV-, they have tuberculosis. An HIV+ measured patient has AIDS (tuberculosis is AIDS defining, see above). With catastrophic consequences for the therapy, since these people are treated not only against tuberculosis, but especially with HAART against HIV and all degenerative phenomena of the organism associated with it.

- Sadiq et al., "*Adverse Drug Reaction Profile in Patients on Anti-tubercular Treatment Alone and in Combination with Highly Active Antiretroviral Therapy*.", J Clin Diagn Res. **2015** Oct;9(10):FC01-4, https://www.ncbi.nlm.nih.gov/pubmed/26557538

*"On comparison, ADE rate of TB with HIV co-morbid patients was more (**55.8%**) than TB patients (**0.36%**) (p < 0.001)."*

*"**The study underscores that concomitant HAART and ATT, result in more ADRs in comparison to ATT alone** demanding collaboration & integration of National AIDS Control programme and PvPI to enhance drug safety in this field."*

- Yimer et al., "*Evaluation of patterns of liver toxicity in patients on antiretroviral and anti-tuberculosis drugs: a prospective four arm observational study in ethiopian patients.",* PLoS One. **2014** Apr 8;9(4):e94271, https://www.ncbi.nlm.nih.gov/pubmed/24714066

*"Concomitant anti-TB-HIV therapy increased the risk of DILI by **10-fold** than anti-TB alone (p<0.0001). HIV co-infection increased the risk of anti-TB DILI by **4-fold** (p = 0.004). HAART associated DILI was **3-fold** higher than anti-TB alone, (p = 0.02)."*

However, the correlation between HIV+ and AIDS is always 100% - by definition.

But, at least in the early years until the early 1990s, years after the announcement of *HIV = AIDS*, AIDS without HIV had been accepted to increase statistics. This surprising circumstance will be discussed below.

Statistics also confound cause (causality) and correlation. An example: Kaposi's sarcoma (KS) is a very rare skin cancer (about 5 cases per 1,000,000 inhabitants) without HIV+. KS is AIDS-defining.

In the 1980s KS increasingly appeared among homosexual men, mostly strong Popper's users, cf. as witnesses from this time

- John Lauritsen, Hank Wilson, „Death Rush: Poppers and AIDS“, **1986** http://paganpressbooks.com/jpl/POPPERS.HTM

„96-100% of the gay men with AIDS used poppers, usually quite heavily." (page 10)

The men covered with skin lesions became synonymous with AIDS, cf.

- Curtiss et al. *„An Update on Kaposi's Sarcoma: Epidemiology, Pathogenesis and Treatment*", Dermatol Ther (Heidelb) **2016** Dec; 6(4): 465–470, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5120640/

But In the biopsy of KS cells no retroviral DNA (provirus) is found, cf.

- Delli Bovi et al. „*Presence of Chromosomal Abnormalities and Lack of AIDS Retrovirus DNA Sequences in AIDS-associated Kaposi's Sarcoma*", Cancer Res. 46, 6333-6338, Dec **1986**, https://www.ncbi.nlm.nih.gov/pubmed/3022918

*"Taken together these results suggest that **neither the AIDS retrovirus, HBV, or CMV is required for the altered growth properties of KS cells**."* (page 6334/6335)

Further studies on Kaposi's sarcoma in **HIV-negative, young men**, cf.

- Lanternier et al., *"Kaposi's sarcoma in HIV-negative men having sex with men."*, AIDS. **2008** Jun 19;22(10):1163-8, https://www.ncbi.nlm.nih.gov/pubmed/18525262

„We included HIV-negative homosexual and bisexual male patients with histologically proven Kaposi's sarcoma in a retrospective study."

*"Kaposi's sarcoma may develop in homosexual or bisexual men **without HIV infection**. This type of Kaposi's sarcoma has clinical features in common with classical Kaposi's sarcoma but occurs in younger patients."*

- Friedman-Kien et al., "*Kaposi's sarcoma in HIV-negative homosexual men*.", Lancet. **1990** Jan 20;335(8682):168-9, https://www.ncbi.nlm.nih.gov/pubmed/1967458

However, which is very surprising, suspected HIV proteins can be detected in these individuals without these persons being HIV+, cf.

- Bowden et al. , "*Antibodies to gp41 and nef in otherwise HIV-negative homosexual man with Kaposi's sarcoma*.", Lancet. **1991** Jun 1;337(8753):1313-4, https://www.ncbi.nlm.nih.gov/pubmed/1674298

*"**A homosexual man with histologically confirmed Kaposi's sarcoma remained seronegative for HIV-1, HIV-2, and HTLV-1 on conventional tests over a 4-year period**. HIV cultures were also negative on thirteen separate occasions. However, serum antibodies to synthetic peptide analogues of the gp41 and nef regions of HIV-1 were consistently detected on an enzyme immunoassay. **Tests with the polymerase chain reaction with primers directed to the gag and env regions were negative."***

None of the numerous HIV studies and statistics can distinguish between the cause HIV+ and other possible causes, e.g. discriminate against drug use (Poppers, Ecstacy, Chemsex) or simple malnutrition. Today one would look at PCR and at a magnification of 1,000,000,000x (about 2^{30}) one will always find something retroviral, e.g. HERV. But if you need PCR, the concentrations are very, very low, and doubts about causality are appropriate.

As soon as healthy persons from non-risk groups start HAART therapy, **they will show the expected symptoms after a certain time** (see above). These are then attributed to the suspected disease.

See above and,

- AP, "*Woman Misdiagnosed With HIV Awarded $2.5M*", December 13, **2007**, https://www.cbsnews.com/news/woman-misdiagnosed-with-hiv-awarded-25m/

*"A jury has awarded $2.5 million in damages to a woman who received **HIV treatments for almost nine years** before discovering she never actually had the virus that causes AIDS."*

*"In her lawsuit against a doctor who treated her, Audrey Serrano said the powerful combination of drugs she took triggered a string of ailments**, including depression, chronic fatigue, loss of weight and appetite and inflammation of the intestine.**"*

Weight-loss is AIDS-defining.

This may take years at the rather low doses of HAART today. There is no statistical approach that discriminates between suspected disease and adverse drug reactions. And, as before, only intravenous drug use is statistically recorded, i.e. the problem is the needle is not the drug.

Here is a word of warning required. There are increasingly studies published that point to a correlation between HIV+ and drugs. Whether or not there is a correlation, this is irrelevant to the question of whether or not drugs can trigger **AIDS** as soon as one mentally separates **AIDS** from what is called HIV+. A correlation of HIV+ and drugs only points to a risky behavior, which is also reflected by the high correlation between HIV+ and for example syphilis and herpes. On the other hand, there is not the slightest doubt about the correlation between drugs and AIDS in the original AIDS population in San Francisco.

Because of the widespread prevalence of retroviral activities even in healthy people (see below, HERV), I am very skeptical as to whether diagnostic discrimination will be possible. After 35 years of thinking **HIV equals AIDS**, it will be very difficult to come back to an objective question.

15.1. AIDS without HIV

Can you actually have AIDS without being HIV+?

Yes, according to the case definitions for statistics one can.

At least when it comes to the original AIDS case definitions of the CDC from the US. But it is precisely the statistics that have been used to *prove* in 1984 the HI virus theory of AIDS.

It turns out that at that time the HIV status of the majority those multiple-infected, drug-addicted men in San Francisco and New York was not known. Cf.

- CDC, Center for Disease Control, "*Revision of the CDC surveillance Case Definition for Acquired Immunodeficiency Syndrome*" MMS Supplement, August 14, **1987**, Vol. 36, No. 1S, https://www.cdc.gov/mmwr/pdf/other/mmsu3601.pdf

"The effectiveness of the revision will depend on how extensively HIV-antibody tests are used. Approximately one third of AIDS patients in the United States have been from New York City and San Francisco where, ***since 1985, < 7% have been reported with HIV-antibody test results****, compared with > 60 % in other areas."*

In the epicenter of AIDS, New York City and San Francisco, <7% with HIV test results? How could one even develop a theory based on this data? And this number says only something about the number of tests, and nothing to the number of actually infected. This becomes clear when one asks what we mean by "*standard of good medical practice*". At least not these case definitions, cf. ibid

*"****The diagnostic criteria accepted by the AIDS surveillance case definition should not be interpreted as the standard of good medical practice****. Presumptive diagnoses are accepted in the definitions because not to count them would be to ignore substantial morbidity resulting from HIV infection."*

What is the point of talking about "*morbidity, resulting from HIV infection*" if you have tested <7% of people in the centers of the alleged epidemic?

For the statistics one accepts all values, but then worries about the individual *patient*. Where is the connection between the suspected *patient* and the statistics?

Cf. also ibid.

„For national surveillance purposes, ***the tiny proportion of possibly false-positive screening test in persons with AIDS indicative disease is of little consequence****. For the individual patient, however, a* ***correct diagnosis is critically important****. The use of supplemental tests is, therefore, strongly endorsed."*

Given the very low positive predictive value (PPV, see Annex I) of HIV tests of <1% in non-risk groups, as well as the numerous false positives by numerous classical pathogens, it would have been very appropriate to establish the exact relationship between the *patient* and statistics. This would have been important also because of the numerous classical infections found in high-risk groups that are cross-reactive to HIV tests, see above.

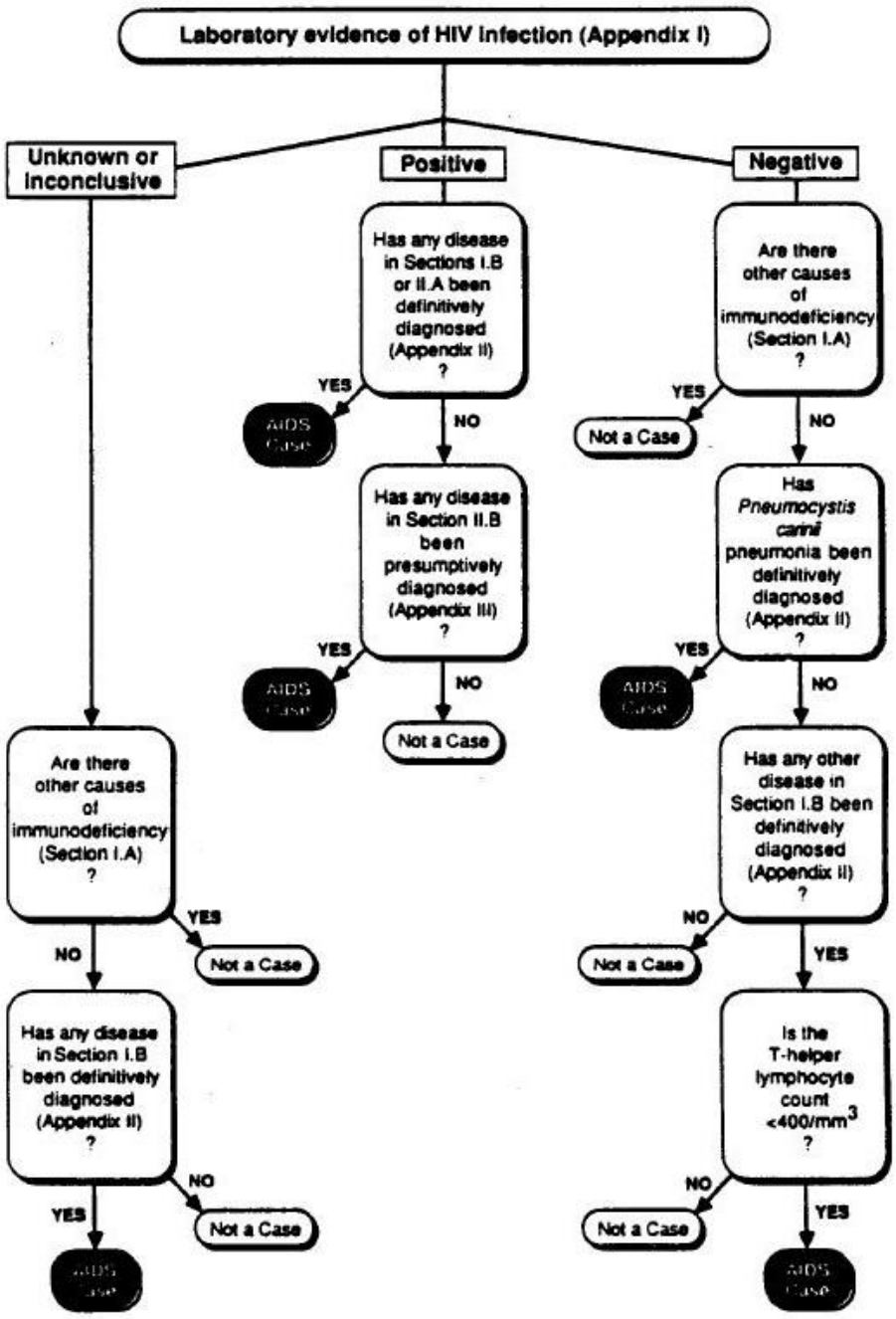


*Figure: Flow diagram for revised CDC case definition of AIDS, September 1, 1987, from CDC, MMS Supplement, August 14, **1987**, Vol. 36, No. 1S*

But this makes it easier to define an infectious epidemic. And one does not even need a new virus. A classical infection, e.g. Tuberculosis, and weight loss due to prolonged diarrhea along with a low CD4 cell count (less than 400 / mm3) suffices to define an ***HIV-negative AIDS case***, see figure above.

As we have seen above, the CD4 cell count is decreased in many classical infections.

In 1984, in a press conference (Heckler and Gallo), the alleged cause of AIDS had been presented, namely HIV, whereas in 1987 in the AIDS case definitions a low CD4 cell count also in case of HIV- was sufficient. What consequences did this have, e.g. in Africa? Has in every single case further analysis been performed?

Or have people been treated with AZT and since 1996 with HAART and the subsequent death of the patient has been taken as proof of the virus hypothesis?

But these are the statistic definitions that have been used to prove the pathogenicity of the putative HI virus. And that's what it's all about: is HIV the cause of AIDS? According to these case definitions, this question can also be answered in the following way: yes, if we attribute all other causes to the HI virus as well.

But there is a system behind the procedure shown here. If one looks at the original works, it becomes clear that already there the proof of a HI virus was not successful ***in more than half of the cases***, cf.

- Gallo et al., "*Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS.*", Science. **1984** May 4;224(4648):500-3, https://www.ncbi.nlm.nih.gov/pubmed/6200936

Diagnosis*	Number positive for HTLV-III	Number tested	Percent positive
Pre-AIDS	18	21	85.7
Clinically normal mothers of juvenile AIDS patients	3	4	75.0
Juvenile AIDS	3	8	37.5
Adult AIDS with Kaposi's sarcoma	13	43	30.2
Adult AIDS with opportunistic infections	10	21	47.6
Clinically normal homosexual donors	1	22	4.5
Clinically normal heterosexual donors	0	115	0

*With the exception of the normal heterosexual donors and some of the clinically normal mothers of juvenile AIDS patients, all others belong to one of the groups of people identified as being at risk for AIDS (homosexual males, intravenous drug users, Haitian immigrants, heterosexual contacts of members of a group at risk, hemophiliacs treated with pooled blood products, recipients of multiple blood transfusions, and infants born of parents belonging to other groups at risk). Pre-AIDS includes patients with unexplained chronic lymphadenopathy and leukopenia, with an inverted T4 (helper)/T8 (suppressor) lymphocyte ratio. The clinically normal, nonpromiscuous, homosexual subjects are from Washington, D.C., and are believed to be at moderate risk. The clinically normal heterosexual donors include both male and female subjects believed not to be at risk for AIDS.

The so-called HI virus was undetectable in adults with Kaposi's sarcoma in 70% of the cases.

Of course, these experiments were also performed on **activated cells** (here by PHA, Phytohemagglutinin). In popular-scientific article this is stated then as "*researchers found that ...*".

15.2. CD4 cell count as *AIDS criteria*

In 2009, AIDS statistics were (again) redefined and **AIDS** itself now declared **HIV Stage III**. This opens 2 stages (I and II) for non-AIDS but HIV-related diseases. That means the WHO catalog of about 30 AIDS-defining diseases is still valid (now HIV Stage III). But there are also other diseases that are now to be assigned to the HI virus.

Cf. the CDC case definitions,

- CDC, "*HIV Infection (AIDS Has Been Reclassified As HIV Stage III) (AIDS/HIV)*", **2009**, https://wwwn.cdc.gov/nndss/conditions/hiv-infection/

- CDC, "*Revised Surveillance Case Definition for HIV Infection — United States, 2014*", April 11, **2014**, https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6303a1.htm

In the new, redefined version of AIDS (now HIV Stage III) and HIV (Stage I and II), the CD4 cell count becomes even more important. This very questionable indicator is now crucial.

*„[TABLE. HIV infection stage]The stage **is based primarily on the CD4+ T-lymphocyte count**; the CD4+ T-lymphocyte count takes precedence over the CD4 T-lymphocyte percentage, and the percentage is considered only if the count is missing. There are three situations in which the stage is not based on this table:*

1) if the criteria for stage 0 are met, the stage is 0 regardless of criteria for other stages (CD4 T-lymphocyte test results and opportunistic illness diagnoses);

*2) if the criteria for stage 0 are not met and a stage-3-defining opportunistic illness has been diagnosed (Appendix), **then the stage is 3 regardless of CD4 T-lymphocyte test results**;"*

At the same time, one lowers the threshold for the diagnosis of AIDS-defining infections (opportunistic infections), ibid,

"*The diagnosis of any of the opportunistic illnesses, irrespective of diagnostic method used, will meet the criteria for staging, **thereby eliminating the requirement in the 2008 case definition for some of them to be "definitively" diagnosed**.*"

This undoubtedly leads to a further increase in case numbers.

Cf. also

- WHO, "*WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children*.", **2007**, https://www.who.int/hiv/pub/guidelines/HIVstaging150307.pdf

"Box 2. Criteria for diagnosis of advanced HIV (including AIDS) for reporting

Clinical criteria for diagnosis of advanced HIV in adults and children with confirmed HIV infection: presumptive or definitive diagnosis of any stage 3 or stage 4 condition

and/or;

Immunological criteria for diagnosing advanced HIV in adults and children five years or older with confirmed HIV infection:

***CD4 count less than 350 per mm3 of blood in an HIV-infected adult or child**.*

and/or;

Immunological criteria for diagnosing advanced HIV in a child younger than five years of age with confirmed HIV infection:

%CD4+ <30 among those younger than 12 months;
%CD4+ <25 among those aged 12–35 months;
%CD4+ <20 among those aged 36–59 months."

Summary:

- What we get is HIV statistics, not AIDS statistics.
- Decisive for AIDS is the CD4 cell count, which has no significance, but
- any other diseases are included in it, e.g. tuberculosis

15.3. So called *HIV-related diseases*

The introduction of HIV Stages I, II and III (AIDS) and the associated complexity of the diagnosis certainly leads to a further increase in case numbers, as was the case for the earlier statistical redefinitions. The emphasis on the questionable CD4 cell count is also in direct contrast to the publications which see the CD4 cell count decreased in the context of numerous lighter and more severe infections.

In addition, the discussion is shifting from *"HIV = AIDS"* (the dogma) to *"HIV, yes or no?"* The problem is that HIV is now directly responsible, i.e. not supposedly by switching off the immune system (especially CD4+ cells), but to act by the direct infection of other cells.

This leads to a wealth of different diseases, such as **diabetes**, **osteoporosis**, **cardiovascular diseases**, **dementia**, **liver damage** and **cancer**, which are now supposedly caused by HIV directly, see above and cf.

- Deeks et al., "*The End of AIDS: HIV Infection as a Chronic Disease*", Lancet. **2013** Nov 2; 382(9903): 1525–1533, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4058441/

*„Studies conducted in high income countries tell us that HIV-infected adults experiencing durable treatment-mediated suppression of HIV replication are at risk for developing a number of **non-AIDS conditions**, including **cardiovascular disease, cancer, kidney disease, liver disease, osteopenia/osteoporosis** and **neurocognitive disease** (collectively referred to as "**serious non-AIDS events**")."*

Comment: HIV-infected people refers to people on HAART, „*experiencing durable **treatment-mediated** suppression of HIV replication*".

These are amazingly different diseases for such a small virus with about 8,000 base pairs. In addition, it should also, somehow, lead to a dying of the CD4 + cells (see below on the *bystander cell problem*).

The alleged evidence of HIV influence on the respective tissue is always carried out by **activated cells** (see above), which should show reverse transcriptase activity. This is then interpreted as a HI virus infection of the cells.

What is behind this?

For one thing, there are far too few AIDS cases for an **AIDS epidemic**. According to the original estimates from the 80s and 90s, we would have today climb over mountains of corpses of female prostitutes, which we do not.

HAART cannot be the cause, because **HAART cannot cure AIDS**. HAART is supposed to prevent the onset of AIDS. But what if people die without first getting AIDS? Then you would have a problem with *HIV = AIDS* alone.

On the other hand, there are massive problems with the *slow virus* concept and the multi-year latency and the human antibodies. A virus multiplies in the rhythm of cell division. This is rather fast and takes a few days. How do you explain the years after that, when nothing happens?

This results in the difficulty to make a population swallow these severe cytotoxins, if the consequences of an infection with the putative HIV virus are to appear only years later.

So there is a gap. This one tries to fill with *HIV-related diseases*. This refers to diseases that do not correspond to the opportunistic infections of an immunosuppressed person, but that are independent of it.

However, the aforementioned HIV-related diseases are 100% identical to the observed side effects of HAART, as is shown among others by the cases of misdiagnosed, HIV-negative people.

15.4. HIV/AIDS statistics: what is missing?

In addition to the serious problems of HIV / AIDS statistics, such as the CD4 cell count as an unusable bio-marker, the difficult data collection in Africa (see below), the confusing definition of AIDS with about 30 long-known diseases, the strong negative effects of HAART Therapy as well as classical infections, which are hardly considered as soon as the person has been measured HIV+, there is another crucial problem with the statistics.

It concerns the infection rate of a sexually transmitted disease.

In a classical infection, the more infected there are, the more people become infected. The contact probability and thus the likelihood of transmission is the greater, the more infected there are. That means the infection rate is proportional to the number of infected people. This leads mathematically at the beginning of an epidemic to an exponential growth of the number of infected people.

One has to make a clear distinction here. This is (initially) not about a disease (AIDS), but it is about the infection with a new, putative virus (HIV), that newly arrived in a hitherto allegedly not infected population. Then, in the beginning, in the spread, i.e. in the infection rate, an exponential increase must show up.

At the same time there are normally limiting factors that lead later to the formation of a stationary state, i.e. a flat curve.

On the one hand, there are mutations that inactivate the pathogen. And the putative HI virus is the fastest mutating pathogen currently known to science, cf.

- Cuevas et al., "*Extremely High Mutation Rate of HIV-1 In Vivo*", Published online **2015** Sep 16, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4574155/

„This reveals an extremely high mutation rate of (4.1 ± 1.7) × 10^{-3} per base per cell, ***the highest reported for any biological entity****. Sequencing of plasma-derived sequences yielded a mutation frequency 44 times lower, indicating that a large fraction of viral genomes* ***are lethally mutated and fail to reach plasma****. "*

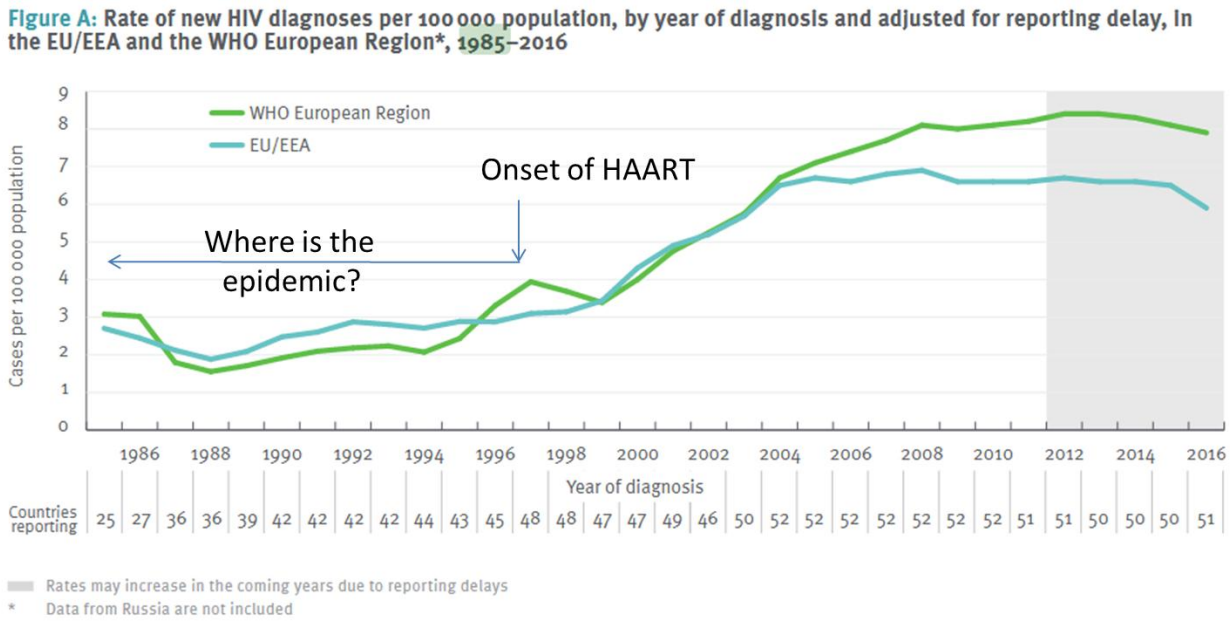
In addition, there is the immunization against the pathogen, which has a limiting effect, since an immunized person cannot be infected a second time. He has made antibodies against the pathogen. Along with the immunization, the distribution also decreases because an immunized person can no longer infect others after a certain time. For example, chickenpox, although many adults had chickenpox in their childhood and also can get shingles, they can no longer transfer the chickenpox to others.

Thus, after some time, which can be several millennia or more, the infection rate remains constant.

What does the data show for HIV?

The HIV diagnosis rate is considered to approximate the actual HIV infection rate. It should also be noted that these data are primarily related to risk groups in which the putative HI virus is measured more often than in non-risk groups. Cf.

- ECDC, "*HIV/AIDS surveillance in Europe 2017 - 2016 data, surveillance report*", 28 Nov **2017**, https://www.ecdc.europa.eu/sites/portal/files/documents/20171127-Annual_HIV_Report_Cover%2BInner.pdf



(Figure: HIV diagnosis rate 1985 - 2016, the mark "Onset of HAART" is for guidance only.)

One can see a nearly flat curve for the years before 1996, which even dropped between 1985 and 1988. Over the next 10 years, there is a slight increase until at the end of the 2000s a plateau seems to be emerging anew.

Where is the exponential rise in the early years, that is in the 80s?

The use of HAART around 1996 serves only as an orientation, since HAART plays no role in the infection. But it is also the time when HIV / AIDS started on an industrial scale.

Strangely enough, the diagnoses start to increase from this point on, **but that is far too late**. One must not forget, antibodies allegedly do not work for HIV. At the same time science assumes that every mutation of the putative HI virus is pathogenic and escapes equally the immune system.

Thus, there is nothing limiting that could have slowed down the exponential spread of the putatively new pathogen in an unprotected population in the early years.

However, the exponential increase, characteristic of a new sexually transmitted disease, is completely missing. And we mainly talk about risk groups (MSM), with up to several hundred different sexual partners per year in the 80s. A pathogen (without effective antibodies) could have spread arbitrarily.

However, the flat curve in the period before 1996 strongly suggests that there were limiting factors. That means inactivating mutations as well as anti-bodies play an important role, as with all other viruses, pathogenic or non pathogenic. Additionally, the flat curve in these years shows that nothing is newly spreading. But we talk about a pathogen or phenomenon that has been around for a long time. The stationary state has already been reached.

The late rise from the end of the 90s on indicates rather that many have jumped on the bandwagon. How could it be otherwise, after each hospital had its HIV center funded? It is to be feared that the large number of false positives that serological tests but also PCR produce has contributed to the increased number of diagnoses compared to the 1980s. The true infection rate would then be lower than the (observable) rate of diagnosis.

From the HIV statistics, thus the alleged spread of a putative pathogen, the AIDS statistics is to be distinguished. The later refers to diagnosis of the about 30 catalog diseases of the WHO and the main criterion "*CD4 cell count*", which is extremely questionable.

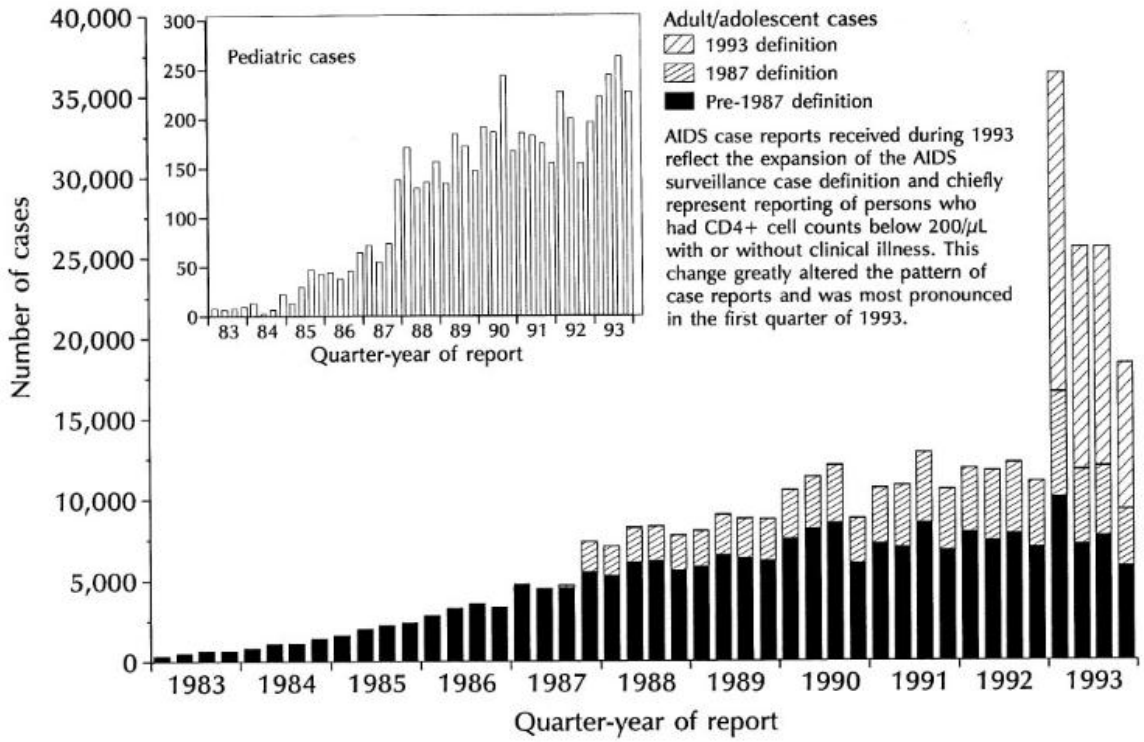
It is to be expected that AIDS statistics contain even greater uncertainties (such as estimates) than HIV statistics. However, looking at AIDS statistics in the US in the early years, two things stand out:

a) the influence of the criteria changes on the AID syndrome case numbers
b) the missing exponential increase.

Cf.

- CDC, HIV/AIDS Surveillance Report, "*U.S. HIV and AIDS cases reported through December 1993*", **1993**, Year-end Edition, Vol. 5, No. 4, https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-1993-vol-5-4.pdf

From this figure 6.



(Figure 6. AIDS cases by quarter-year of report and definition category, reported 1983 through 1993, United States)

It is one of the few statistics that splits the AIDS case numbers at least according to criteria catalog. After 1993, I found no such representation.

It can be clearly seen that the AIDS case numbers for adults (*adult/adolescent cases*) after the *pre-1987* as compared to the *1987* definition from about 1988 are almost constant. This is far ahead of HAART, which was available from about 1996. The same applies, with greater variability for the children (*pediatric cases*).

Only the case definitions of AIDS from 1993 lead to a significant increase, which then immediately decreases again. In the 1993 criteria of AIDS the CD4 cell number is included, see inset:

„AIDS case reports received during 1993 reflect the expansion of the ADIS surveillance case definition and chiefly represent reporting of persons ***who had CD4+ cell counts below 200/µL with or without clinical illness.****"*

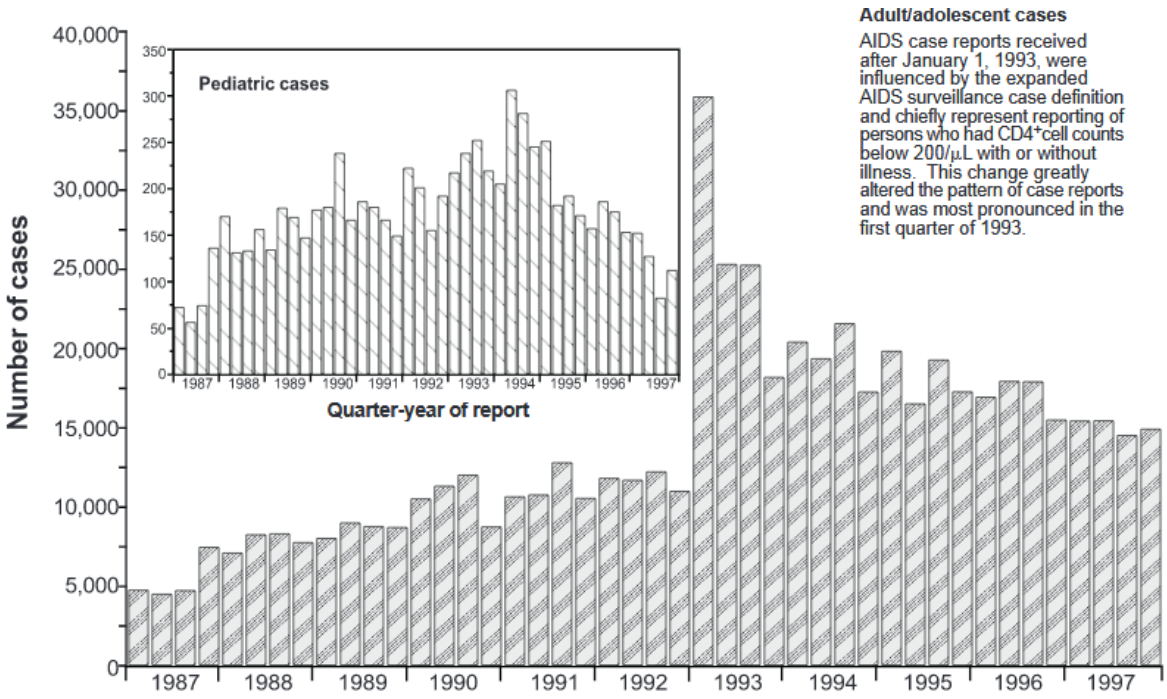
"*With or without clinical illness*", this reference is often missing in the information and the population automatically associates AIDS with the dying people from Africa. Today in the US and Europe healthy people are shown, thanks to HAART.

However, even the original statistics show that people with low CD4 cell counts do not need to be immunosuppressed, especially outside of high-risk groups and without classical infection, see also above for the misdiagnosed cases, Ms. Suthida Saengsumat, and below on the CD4 cell count.

And again the question: where is the exponential increase of a sexually transmitted disease in the early years?

This breakdown after AIDS case definition catalogs is missing in later statistics. I find the last curve of this kind (without splitting according to AIDS case catalogs) for 1997, cf.

- CDC, HIV/AIDS Surveillance Report, "*U.S. HIV and AIDS cases reported through December 1997*", **1997**, Year-end Edition, Vol. 9, No. 2, https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-1997-vol-9-2.pdf



(Figure 6. AIDS cases by quarter-year of report and age group, reported 1987 through 1997, United States)

Even after the new AIDS case catalog a drop from 1993 can be seen. However, this is usually attributed to HAART, which, however, was only available from 1996 onwards. It is simply claimed that the disease is under control, thanks to HAART.

These people are defined *sick*, meanwhile predominantly on the basis of their CD4 cell number. This is not an epidemic.

16. Inflation of HERV[5]

The topic has already been addressed when talking about the cross reactions of the HIV Ag / Ab tests. In human cells, residual levels of retroviruses (HERV) can be detected, which are said to have found their way into the human genome in the course of evolution, cf.
https://en.wikipedia.org/wiki/Endogenous_retrovirus#Human_endogenous_retroviruses

Of course, it is somewhat questionable to call these gene sequences "*endogenous viruses*" since no one has 1 million years ago observed the infection. The problem is that these HERV genes comprise about 8% of the human genome. As it turns out, HERV, or better, the assumed retroviral activity appears in many places. One can speak of an inflation of HERV. Below are some references given:

HERV and multiple sclerosis
HERV and schizophrenia
HERV and rheumatic arthritis
HERV and type 1 diabetes mellitus
HERV and psoriasis
HERV and cancer
HERV and placenta
HERV and HIV

HERV and multiple sclerosis

- Bhetariya, P. J., „*Analysis of Human Endogenous Retrovirus Expression in Multiple Sclerosis Plaques*“, J. Emerg. Dis. Virol. **2017** August ; 3(2): (Author Manuscript), https://www.ncbi.nlm.nih.gov/pubmed/28868516

- Dolei, A., „*The aliens inside us: HERV-W endogenous retroviruses and multiple sclerosis*“, Multiple Sclerosis Journal **2018**, Vol. 24(1) 42–47, https://www.ncbi.nlm.nih.gov/pubmed/29307292

- Morandi, E., „*Human endogenous retroviruses and multiple sclerosis: Causation, association, or after-effect?*“, Multiple Sclerosis Journal **2017**, Vol. 23(8) 1050–1055 https://www.ncbi.nlm.nih.gov/pubmed/28406354

HERV and schizophrenia

- Christensen, „*HERVs in neuropathogenesis.*“, J Neuroimmune Pharmacol. **2010** Sep; 5(3):326-35, https://www.ncbi.nlm.nih.gov/pubmed/20422298

HERV and rheumatic arthritis

- Ejtehadi et al. „*The potential role of human endogenous retrovirus K10 in the pathogenesis of rheumatoid arthritis: a preliminary study.*“ Ann Rheum Dis. **2006** May;65(5):612-6,

[5] HERV here refers to the presence of retroviral activity (i.e., reverse transcriptase activity).

https://www.ncbi.nlm.nih.gov/pubmed/16192292

- Nexø et al., *„Are human endogenous retroviruses triggers of autoimmune diseases? Unveiling associations of three diseases and viral loci*." Immunol Res. **2016** Feb;64(1):55-63, https://www.ncbi.nlm.nih.gov/pubmed/26091722

HERV and diabetes

- Bashratyan, R. et al., *„Type 1 diabetes pathogenesis is modulated by spontaneous autoimmune responses to endogenous retrovirus antigens in NOD mice*", Eur. J. Immunol. **2017**. 47: 575–584, https://www.ncbi.nlm.nih.gov/pubmed/28083937

HERV and psoriasis

- Molès et al., *"A new endogenous retroviral sequence is expressed in skin of patients with psoriasis*.", Br J Dermatol. **2005** Jul;153(1):83-9, https://www.ncbi.nlm.nih.gov/pubmed/16029331

- Molès et al. "*Cytosolic RNA: DNA Duplexes Generated by Endogenous Reverse Transcriptase Activity as Autonomous Inducers of Skin Inflammation in Psoriasis*.", PLoS One. **2017** Jan 17;12(1):e0169879, https://www.ncbi.nlm.nih.gov/pubmed/28095445

- Lättekivi et al., "*Transcriptional landscape of human endogenous retroviruses (HERVs) and other repetitive elements in psoriatic skin*.", Sci Rep. **2018** Mar 12;8(1):4358, https://www.ncbi.nlm.nih.gov/pubmed/29531256

HERV and cancer

See also above, Rakowicz-Szulczynska et al. on breast and prostate cancer in HIV-negative persons. It should not be forgotten that there are also AIDS-defining cancers. However, here we talk about cancer and HERV in *HIV-negative persons*. However, the question arises as to whether cancer itself produces a retroviral signal and how to differentiate it from HIV.

- Johanning, G., et al. *„Expression of human endogenous retrovirus-K is strongly associated with the basal-like breast cancer phenotype*", Sci. Rep. **2017**, 7, 41960, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5292751/

- Callahan et al., "*A new class of endogenous human retroviral genomes*.", Science. **1985** Jun 7;228(4704):1208-11, https://www.ncbi.nlm.nih.gov/pubmed/2408338

"Human DNA contains multiple copies of a novel class of endogenous retroviral genomes."

"Nucleotide sequence analysis revealed regions in the HLM-2 pol gene that were as much as 70 percent identical to the mouse mammary tumor virus pol gene."

- Golan et al., "*Human Endogenous Retrovirus (HERV-K) Reverse Transcriptase as a Breast Cancer Prognostic Marker*", Neoplasia. **2008** Jun; 10(6): 521–533, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2386537/

"The presence of HERV-K-T47D-RT was further tested in human breast tumors. We have shown that the HERV-K-RT protein is expressed in 26% of breast carcinoma cases tested (28/110) and in 18% of adjacent normal tissue tested (15/85)."

"These data correlate with the previously published results showing that HERV-K ENV is expressed in 45% of the breast tumors and in 18% of the adjacent normal tissue."

- Wang-Johanning et al., "*Expression of human endogenous retrovirus k envelope transcripts in human breast cancer.*", Clin Cancer Res. **2001** Jun;7(6):1553-60, https://www.ncbi.nlm.nih.gov/pubmed/11410490

"In contrast, HERV-K transcripts were detected in most breast cancer cell lines and many breast tumor tissues. Expression was detected in a small percentage of matched, uninvolved breast tissues and in placentas but not nonmalignant breast tissues. In HERV-K-positive breast cancer tissues, Northern blot analysis demonstrated full-length proviral and spliced env transcripts."

"Independently isolated clones of HERV-K env cDNA generated recombinant proteins of the expected size. Sequence analysis of env cDNA clones derived from four breast tumor samples ***revealed >97% identity with the type I HERV-K102, with no premature termination codons****. Independent isolates from the same breast tumor sample showed nucleotide sequence differences, suggesting that multiple loci may be transcribed."*

"These data indicate that HERV-K transcripts with coding potential for the envelope region are expressed frequently in human breast cancer."

- Downey et al., "*Human endogenous retrovirus K and cancer: Innocent bystander or tumorigenic accomplice*?", Int J Cancer. **2015** Sep 15; 137(6): 1249–1257, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6264888/

"However, ***the discovery of high levels of HERV-K mRNA*** *and protein and even virions in a wide array of cancers has revealed that HERV-K may be playing a more sinister role–a role as an etiological agent in cancer itself. Whether the presence of this retroviral material is simply an epiphenomenon, or an actual causative factor, is a hotly debated topic."*

- Gonzalez-Cao, "*Human endogenous retroviruses and cancer*.", Cancer Biol Med. **2016** Dec;13(4):483-488, https://www.ncbi.nlm.nih.gov/pubmed/28154780

"However, a correlation between HERVs and human cancer has been described and many tumors, such as ***melanoma****,* ***breast cancer****,* ***germ cell tumors****,* ***renal cancer*** *or* ***ovarian cancer****, express HERV proteins, mainly HERV-K (HML6) and HERV-K (HML2). Although the causative role of HERVs in cancer is controversial, data from animal models demonstrated that endogenous retroviruses are potentially oncogenic."*

The findings on HERV and cancer even reached the Robert Koch Institute (RKI) in Germany, cf.

- Bannert et al., "*HERVs New Role in Cancer: From Accused Perpetrators to Cheerful Protectors*", Front Microbiol. **2018**; 9: 178, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5816757/

"It has been recognized for many years that endogenous retroviruses and other retroelements contribute to malignant diseases as well as to inflammatory and autoimmune disorders at the DNA and presumably at the protein level. However, until recently, it escaped attention that an increased expression of HERV-derived nucleic acids also has an adverse effect on cancer cells and that this effect could be the basis of novel therapeutic approaches."

I am not aware that in recent decades the RKI has once addressed the question of how to distinguish between endogenous and exogenous contributions of putative retroviral activity. The contradictions in the HI virus hypothesis of AIDS still persist, but one is already progressing to *novel therapeutic approaches*.

- Sacha et al., "*Vaccination with cancer- and HIV infection-associated endogenous retrotransposable elements is safe and immunogenic*.", J Immunol. **2012** Aug 1;189(3):1467-79, https://www.ncbi.nlm.nih.gov/pubmed/22745376

*"**HIV-1 infection triggers HERV-K RNA and protein expression** since antibody responses to HERV-K are more commonly found in HIV-1 infected persons (21–24)."*

- van der Kuyl, "*HIV infection and HERV expression a review*", Retrovirology **2012**, 9:6 https://retrovirology.biomedcentral.com/articles/10.1186/1742-4690-9-6

"*One HIV-induced change is the induction of HERV transcription, often leading to induced HERV protein expression."*

It seems somewhat strange that an exogenous retrovirus initiates the expression of an endogenous retrovirus. Which consequence has this for the diagnosis, e.g. the RNA viral load? Is HERV being measured? And should one not first ask what is diagnosed without putative, exogenous retrovirus, e.g. by PCR?

And, does one not confound cause and effect here, namely, that retroviral activity is an expression of stressed cells, cf. also below in oxidative stress?

How do you discriminate the contribution of HERV in HIV+ measured people? And what evidence is there for a chain of effects from the putative HI virus to a disease given the omnipresent, endogenous components?

HERV and placenta

In the context of HERV again the special relation to retroviral activity in the placenta, see above for HIV antibody tests.

- Johansen et al. "*Members of the RTVL-H family of human endogenous retrovirus-like elements are expressed in **placenta***.", Gene. **1989** Jul 15;79(2):259-67, https://www.ncbi.nlm.nih.gov/pubmed/2551777

- Johnson et al., "*Endogenous retroviral expression in the human placenta*.", Am J Reprod Immunol. **1990** Aug;23(4):115-20, https://www.ncbi.nlm.nih.gov/pubmed/1703766

- Nelson et al, "*Normal human placentas contain RNA-directed DNA polymerase activity like that in viruses.*", Proc Natl Acad Sci U S A. **1978** Dec; 75(12): 6263–6267, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC393161/

*"**Extracts from over 100 normal human placentas** have been examined for RNA-directed DNA polymerase (…) activity. More than 80% of these placentas contained this enzyme activity, which banded at a density of 1.15-1.17 g/ml in sucrose. After heat treatment, this enzyme activity was shifted in density to 1.22-1.24 g/ml. The enzymatic activity was greater with $(rC_n)(dG)_{12-18}$ than with $(dC)_n(dG)_{12-18}$ and was not stimulated by $(dG)_{12-18}$ alone. "*

*"Retrovirus-like particles have been detected by electron microscopy in nonhuman and human primate placentas. RDDP activity has been described in normal placental tissue of rhesus monkeys (16) and rabbits (17) and in human amniotic fluid (18). **The experiments described in this paper demonstrate that normal human placental tissue also possesses RDDP activity associated with structures banding at densities characteristic of complete retroviruses and viral cores**. The results indicate that RDDP like that in viruses, previously recognized only in human tumors, can be detected in normal human tissues as well."*

And should this not be investigated further? "***Retrovirus-like particles have been detected by electron microscopy in nonhuman and human primate placentas.**"*

- Chuong , "*The placenta goes viral: Retroviruses control gene expression in pregnancy*.", PLoS Biol. **2018** Oct 9;16(10):e3000028, https://www.ncbi.nlm.nih.gov/pubmed/30300353

*"To conclude, the study by Dunn-Fletcher and colleagues adds to a growing body of evidence supporting a **remarkable evolutionary relationship between retroviruses and the placenta**. A picture is now emerging in which important features of placentation are often reliant on proteins and regulatory sequences co-opted from ancient retroviruses."*

It seems a bit strange that these results are so completely lost, especially when one thinks of the numerous false positives in pregnant women.

HERV and HIV

- Contreras-Galindo, R., "*HIV-1 Infection Increases the Expression of Human Endogenous Retroviruses Type K (HERV-K) in Vitro*", AIDS RESEARCH AND HUMAN RETROVIRUSES, Vol. 23, No 1, **2007**, pp. 116–122, https://www.ncbi.nlm.nih.gov/pubmed/17263641

Antibodies against HERV are also found in> 60% of the HIV+ measured babies:

- Tandon et al., „*Identification of Human Endogenous Retrovirus-Specific T Cell Responses in Vertically HIV-1-Infected Subjects*"; J. Vir., Nov. **2011** , Vol. 85, No. 21,, p. 11526–11531 https://www.ncbi.nlm.nih.gov/pubmed/21880743

"*HERV (-H, -K, and -L family)-specific T cell responses were identified in **26 of 42 subjects**, with the greatest magnitude observed for the responses to HERV-L*."

It is questionable whether the specificity of the tests is sufficient in all cases to distinguish effectively between HERV and HIV.

- Haist et al. „ *Reactivities of HIV-1 gag-Derived Peptides with Antibodies of HIV-1-Infected and Uninfected Humans*", AIDS RESEARCH AND HUMAN RETROVIRUSES, Vol 8, No 11, 1909:1917, **(1992)** https://epub.uni-regensburg.de/20412/1/wolf11.pdf

*"**Amino acid sequence comparison of HIV-1 gag proteins with those of human endogenous retroviruses (ERV K10, ERV 3) revealed significant similarities** predominantly in the domains showing elevated antibody cross-reactions."*

- Horwitz et al, "*Novel human endogenous sequences related to human immunodeficiency virus type 1*", J Virol **1992**. 66:2170-2179, https://www.ncbi.nlm.nih.gov/pubmed/1548756

- Shih et al., "*Detection of Multiple, Novel Reverse Transcriptase Coding Sequences in Human Nucleic Acids: Relation to Primate Retroviruses*", J Virol **1989**. 63:64-75, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC247658/

- Yang et al., "*An ancient family of human endogenous retroviruses encodes a functional homolog of the HIV-1 Rev protein*", Proceedings of the National Academy of Sciences USA, 96 (**1999**) 13404-8, https://www.ncbi.nlm.nih.gov/pubmed/10557333

"*These data provide surprising evidence for an **evolutionary link between HIV-1 and a group of endogenous retroviruses that first entered the human genome approximately 30 million years ago**.*"

It is very surprising that epitopes, i.e. characteristic amino sequences of the putative virus, are found in **normal tissue of HIV-neg. persons**, cf.

- Parmentier et al., "*Epitopes of human immunodeficiency virus regulatory proteins tat, nef, and rev are expressed in **normal human tissue***", American Journal of Pathology, 141 (**1992**) 1209-16, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1886654/

"*A marked staining with* ***anti- HIV-1-tat, anti-nef, and anti-rev, and anti-HIV-2-tat anti-bodies was found in a variety of cell types in different organs from uninfected individuals***."

"*In conclusion,* ***epitopes of HIV regulatory proteins are expressed in normal human tissues****. This phenomenon should encourage the study of the possible expression, characteristics, and function of endogenous retroviral-like elements in human cells*."

What significance does this have for the diagnosis?

There are also hybridization reactions in patients with other diseases who are clearly HIV-:

- Ciampolillo et al., "*Retrovirus-Like Sequences in Graves'disease: Implications For Human Autoimmunity*." The Lancet **1989**. 333:1096-1100, https://www.ncbi.nlm.nih.gov/pubmed/2566049

"*On Southern blotting of DNA extracted from thyroid glands of five patients with Graves' disease, two probes (720 bp and 942 bp) for gag human immunodeficiency virus type 1 (HIV-1) gave a positive hybridisation signal in all samples tested. DNAs from peripheral blood mononuclear cells hybridised with the 720 bp gag HIV-1 probe in three of the five patients,* ***none of whom had antibodies to HIV-1.***"

"*The lack of antibodies to HIV-1 and HTVL-1 in this group of patients, none of whom was "at risk" of these infections or had associated syndromes,* ***is evidence against direct involvement of known retroviruses and suggests that a distinct human retrovirus, closely related to HIV-1,*** *might be involved in the pathogenesis of Graves' disease.*"

Was that HERV?

This seems less the beginning of a new HERV science, because that it is a former retrovirus is pure speculation. Rather, it seems that retroviral activity, i.e. reverse transcriptase activity in the healthy but also in the diseased (and HIV) human body is far more common and normal than previously thought.

It is imperative to examine these results in detail in the context of HIV, too.

17. Bystander cell enigma

This is one of the biggest puzzles of HIV research and therefore the peg of this essay. It is little-known that **only about 5% of the immune system's T cells contain HIV**. The rest are so-called bystander cells. These are normal T cells, but they die also. That means, the uninfected bystander cells die. **How should that work if there is no HIV in it**?

Cf.

- Finkel et al. *„Apoptosis occurs predominantly in bystander cells and not in productively infected cells of HIV- and SIV-infected lymph nodes.*“, Nat Med. **1995** Feb;1(2):129-34, https://www.ncbi.nlm.nih.gov/pubmed/7585008

*“We show here, using in situ labelling of lymph nodes from HIV-infected children and SIV-infected macaques, that apoptosis occurs **predominantly in bystander cells and not in the productively infected cells themselves**.”*

- Muro-Cacho et al. *„Analysis of apoptosis in lymph nodes of HIV-infected persons. Intensity of apoptosis correlates with the general state of activation of the lymphoid tissue and not with stage of disease or viral burden.*“, J Immunol May 15, **1995**, 154 (10) 5555-5566; https://www.ncbi.nlm.nih.gov/pubmed/7730654

*“Taken together, these results indicate that the increased intensity of the apoptotic phenomenon in HIV infection is caused by the general state of immune activation, and **is independent of the progression of HIV disease and of the levels of viral load**”*

- Cloyd et al. “*How does HIV cause AIDS? The homing theory.*”, Mol Med Today. **2000** Mar;6(3):108-11, https://www.ncbi.nlm.nih.gov/pubmed/10689313

*“**The mechanism by which HIV causes depletion of CD4+ T cells in infected individuals remains unknown.** Numerous theories have been proposed, but none can fully explain all of the events observed to occur in patients”*

- Garg, Joshi, „*Host and Viral Factors in HIV-Mediated Bystander Apoptosis*.”, Viruses. **2017** Aug 22;9(8), https://www.ncbi.nlm.nih.gov/pubmed/28829402

“*With a limited number of infected cells and vastly disproportionate apoptosis in HIV infected patients, it is believed that apoptosis of **uninfected bystander cells** plays a significant role in this process.”*

“***The number of HIV infected cells in patients is relatively low** and cannot solely account for the loss of CD4 cells in vivo. Hence, it is believed that the loss of CD4 cells during HIV infection is due to the process of bystander apoptosis induction.”*

*“**Apoptosis mediated by HIV infections is more complex than previously thought**. A role of both host and viral factors in this phenomenon is becoming increasingly evident.”*

- Coffin, Swanstrom, "*HIV Pathogenesis: Dynamics and Genetics of Viral Populations and Infected Cells*", Cold Spring Harb Perspect Med. **2013** Jan; 3(1), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3530041/

"HOW DOES HIV-1 CAUSE AIDS? A*s is apparent from this article and the rest of the collection,* ***in the 25+ years since its discovery****, we have learned an enormous amount about HIV,* ***but we still cannot answer the one big question****: How does HIV-1 cause AIDS?"*

"*Even if we knew the mechanism of HIV-mediated cell killing,* ***we would not know how HIV-1 causes CD4$^+$ T-cell decline and AIDS in humans.*** *The observation that virus and cell turnover rates in various SIVs in their natural hosts (such as SIV_{sm} in sooty mangabeys),* ***which do not progress to AIDS****, are essentially identical to those in humans, who do progress, implies that cell killing alone cannot account for AIDS pathogenesis. Indeed, this result is consistent with the* ***high natural turnover rate of activated effector memory helper T cells, the primary target for HIV-1 infection, on the order of 10^{10} cells per day****, of which only a small fraction are infected after the initial primary infection phase."*

- Whitaker et al. "*Re-assessing the virological approach to HIV pathogenesis: can it explain AIDS as an immunological disease?*", J Theor Biol. **1997** Jul 7;187(1):45-56, https://www.ncbi.nlm.nih.gov/pubmed/9236107

"However, these attributes-singly and in combination-are shown here to be inadequate to explain the latency, immunological damage, and clinical dynamics of the disease of AIDS. ***The virological paradigm cannot explain the disease-free period (clinical latency); the mechanism and dynamics of CD4 T cell loss; the reason for the onset of disease at a given time-point; the relationship of CD4 T cell loss to AIDS-type disease;*** *nor the idiosyncratic constellation of immunological and clinical phenomena that comprise AIDS as a unique syndrome."*

- Legitimo et al. [in Italian], "*Brief analytical review of additional possible mechanisms in the pathogenesis of AIDS*", Pathologica. **1994** Apr;86(2):119-27, https://www.ncbi.nlm.nih.gov/pubmed/7936754

"Nonetheless, a number of important issues concerning the pathogenesis of HIV infection remain unresolved. For example, it remains unclear how CD4+ T cells are lost after HIV infection. ***The low frequency of infected cells seen even in advanced infection implies that a direct cythopathic effect of HIV on infected CD4+ T cells cannot explain their disappearance."***

Comments on the bystander cell enigma

How can it be that with only 5% affected cells and the high rate of new formation of CD4 cells it can lead to a reduction of the CD4 cells? And this in people who have been measured HIV+, but show no AIDS symptoms. The AIDS symptoms may be the indication that the immune system is weakened. This is not the case for people who are only HIV+. At a high rate uninfected CD4 cells are newly formed.

That casts a damning light on the very useful *immune reconstitution syndrome* (IRIS), see above, where the reinserting immune response after HAART is supposed to sicken the patient. Those were probably the side effects of HAART after all.

There are also people from non-risk groups who live for decades (!) without any symptoms. These are the so-called Long-Term Non-Progressors (LTNPs), see below. These people do not participate in antiviral therapies (therapy naive), fortunately, otherwise we would never get to know them as LTNP.

This also supports the statement by Rodriguez et al. as well as Ying et al. (see above) that the measured CD4 cell count has little to no significance.

The above questions accompany the HI virus hypothesis since 1984, i.e. for 34 years. In the meantime, it is only remembered in specialist circles that there are still one or two open points. The public usually does not hear about it. They are only supposed to swallow the HAART medication.

Is this science? I don’t think so. But it's definitely a billion dollar business.

18. Risk groups: co-infections and drugs

The Robert Koch Institute (RKI) has sufficiently demonstrated the asymmetry of HIV infection in Germany. There are about 4 - 5x more men than women HIV+ measured. What does this mean for a suspected epidemic when there are high risk groups and non-risk groups?

At the same time there is no doubt about the correlation of unprotected anal intercourse (MSM), resulting classical infections and drug abuse with HIV in risk groups, cf. HIV book by Hoffmann and Rockstroh or below, Appendix III. More than half of all HIV+ men measured in high-risk groups are co-infected with syphilis.

Added to this is the problem that classical infections have an influence on the diagnosis and therapy control, cf.

- Buchacz et al, "*Syphilis increases HIV viral load and decreases CD4 cell count*", AIDS **2004**, 18:2075–2079, https://www.ncbi.nlm.nih.gov/pubmed/15577629

- Palacios et al., „*Impact of syphilis infection on HIV viral load and CD4 cell counts in HIV-infected patients.*", J Acquir Immune Defic Syndr. **2007** Mar 1;44(3):356-9, https://www.ncbi.nlm.nih.gov/pubmed/17159654

"Syphilis infection was associated with a decrease in the CD4 cell count and an increase in the HIV VL in almost one third of the patients. In this series, more than ***two thirds of the syphilis cases were diagnosed in patients who were previously known to be infected with HIV.****"*

How can that be if PCR was as specific to determine HIV viral load as it is usually claimed?

And is the needle really the problem when it comes to drug abuse, or should we not care about the immunosuppressive effects of the drugs in the syringe?

18.1. Immunosuppressive effects of drugs

Especially the correlation with drug abuse, which also corresponds to the original homosexual community affected by AIDS-defining diseases in the USA, should be cause for intensive research. This research exists, but not in the context of HIV.

- John Lauritsen, Hank Wilson, „*Death Rush: Poppers and AIDS*", **1986** http://paganpressbooks.com/jpl/POPPERS.HTM, p. 10:

„*96-100% of the gay men with AIDS used poppers, usually quite heavily.*"

- US Department of Health and Human Services, „*Drug Abuse and Drug Abuse Research. The Third Triennial Report to Congress from the Secretary, Department of Health and Human Services*", (**1991**) https://files.eric.ed.gov/fulltext/ED348604.pdf, p. 164

„***None of the patients showed clinical evidence of hepatitis or AIDS-related disease**, although 5 of the 21 had a significantly reduced T4:T8 ratio (Donahoe et al. 1988). Studies of T-cell E-rosette formation and of its kinetics were performed (Donahoe et al. 1986). **This and earlier studies described how heroin use significantly depresses overall T-cell E-rosette formation (Donahoe et al., 1987, 1986; Kreek 1989, in press).** However, the rates of T-cell E-rosette formation were significantly higher in heroin addicts who were also abusing cocaine. There was almost complete reversal of the usually observed depression of T-cell E-rosette formation in the cocaine-abusing, heroin-addicted subjects.*“

- Liang et al. „*Opioid System Modulates the Immune Function: A Review*“, Transl Perioper Pain Med. **2016** ; 1(1): 5–13, https://www.ncbi.nlm.nih.gov/pubmed/26985446

“*Dated back to 1979, Wybran’s research reported on the modulation of rosette formation of human T lymphocytes by opioids. **Since then numerous immunomodulatory effects of opioids on T lymphocytes have been reported and reviewed.”***

“***However, a considerable amount of studies has convincingly demonstrated that opioids, especially morphine and its derivatives, are immunosuppressive**.”*

“***Opiate abusers are mostly suffered multiple organ failure**. Impairment of immune function is part of the most severe and frequent complications*.”

- Roy et al. „*Opioid Drug Abuse and Modulation of Immune Function: Consequences in the Susceptibility to Opportunistic Infections*“, J Neuroimmune Pharmacol (**2011**) 6:442–465 https://www.ncbi.nlm.nih.gov/pubmed/21789507

*“**As the body of evidence in support of opioid dependency and its immunosuppressive effects is growing**, it is imperative to understand the mechanisms by which opioids exert these effects and identify the populations at risk that would benefit the most from the interventions to counteract opioid immunosuppressive effects.”*

“***Chronic opioid use and abuse has been documented to severely compromise the immune system and thereby, increase the risk of opportunistic infection** (Roy and Loh 1996; Roy et al. 2006; Friedman and Eisenstein 2004; Dinda et al. 2005).*”

“***Morphine through the MOR, DOR and KOR modulates many aspects of immune cell function**. These include immuno-suppressive effects of immune cell cytokine release, chemokine receptor activation and cell migration.”*

Can it be that this planet has a huge drug problem? With cleaner and more effective drugs in developed countries and dirty, stretched drugs in developing countries?

The fact that "*chemsex*" by homosexual men with frequent unprotected anal intercourse strongly correlates with AIDS-defining diseases should be given much more attention, cf.

- Duesberg et al. „*The chemical bases of the various AIDS epidemics: recreational drugs, anti-viral chemotherapy and malnutrition*.“, J Biosci. **2003** Jun;28(4):383-412 https://www.ncbi.nlm.nih.gov/pubmed/12799487

- Haverkos et al., „*Nitrite Inhalants: History, Epidemiology, and Possible Links to AIDS*", Env. Health. Persp. Vol 102 (10), Oct. **1994**, https://www.ncbi.nlm.nih.gov/pubmed/9644194

Here an ***in vivo*** experiment on nitrites:

- Dax et al., „*Effects of Nitrites on the Immune System of Humans*", in NIDA Research Monograph 83, Health Hazards of Nitrite Inhalants, Ed. Haverkos und Dougherty, **1988**, p. 75, https://archives.drugabuse.gov/sites/default/files/monograph83.pdf

"*Eight **HIV-negative male volunteers** gave informed consent to participate in this study. […] Over 4 days of the second week, each volunteer participated in 13 inhalation sessions (0.18, 0.3, and 0.46 ml amyl nitrite each three times, and four placebo doses). The placebo, banana oil, was included in each inhalation session with or without amyl nitrite*"

"***The results showed that exposure to amyl nitrite can induce changes in immune function even after short exposure to moderate doses**. Several tests of immune function showed an "overshoot" over basal activity at 7 days following nitrite inhalation after an initial immunosuppression."*

- Soderberg, "*T cell functions are impaired by inhaled isobutyl nitrite through a T-independent mechanism*", Toxicology Letters, Vol 70 (3), 15 February **1994**, p. 319-329, https://www.ncbi.nlm.nih.gov/pubmed/8284799

"*Inhalation exposure of mice to isobutyl nitrite at 900 ppm for 45 min per day for 14 days caused serious deficits in T cell-mediated immune responses. Cytotoxic T lymphocyte (CTL) activity was reduced by 36% following the exposure. T cell proliferative responses to mitogenic and allogeneic stimulation were reduced by 37% and 51%, respectively.*"

There is no doubt about the immunosuppressive effects of drugs, especially nitrites. And nitrites produce similar conditions as found in AIDS-defining diseases. The use of drugs and nitrites correlates extremely strongly with the occurrence of AIDS-defining diseases in high-risk populations (see also below, Annex III). And it corresponds to the original population in the 1980s which was first diagnosed with AIDS-defining diseases.

So the problem does not seem to be the needle (apart from other pathogens), but what is in the syringe or what is being inhaled. It would be high time for the Robert Koch Institute (RKI) to expand the statistics on non-intravenous drug use and break it down by type of drug. But that does not happen, because it would violate the unified opinion on HIV / AIDS.

18.2. Nitrites and cancer – especially Kaposi Sarkoma

It is little known, however, that there is a direct link between nitrites and cancer, including Kaposi's sarcoma, which was synonymous with AIDS in the 80s and 90s.

- Dutta et al. "*Long-term nitrite inhalant exposure and cancer risk in MSM*", AIDS. **2017** May 15; 31(8): 1169–1180, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5414542/

"Heavy popper use was associated with increased risk of the composite of virus-associated cancers ***among HIV-uninfected study participants aged 50–70 years*** *in models adjusted for demographics, number of sexual partners, and CD4+ cell counts (IRR, 3.04; 95% CI, 1.01–9.12); further adjustment for HBV/HCV, sexually transmitted infections, smoking, and polydrug use did not attenuate this association (Table 5)."*

- Soderberg, „*Increased tumor growth in mice exposed to inhaled isobutyl nitrite*.", Toxicol Lett. **1999** Jan 11;104(1-2):35-41, https://www.ncbi.nlm.nih.gov/pubmed/10048747

"To determine if exposure to nitrite inhalants could alter tumor growth, syngeneic PYB6 tumor cells were injected into groups of mice. Exposure of these mice to inhaled isobutyl nitrite increased both the tumor incidence and the tumor growth rate by almost 4-fold. Following only five daily exposures to the inhalant, the induction of specific T cell mediated cytotoxicity was inhibited by 36%. Similar inhalation exposures inhibited the tumoricidal activity of activated macrophages by 86%."

- Haverkos, "*Nitrite inhalant abuse and AIDS-related Kaposi's sarco*ma.", J Acquir Immune Defic Syndr. **1990**;3 Suppl 1:S47-50, https://www.ncbi.nlm.nih.gov/pubmed/2395087

"There is sufficient clinical and epidemiological evidence to suggest that HIV infection alone does not cause Kaposi's sarcoma (KS) in AIDS. Several possible "cofactors" have been proposed. ***There are several reasons to consider nitrite inhalants as a plausible choice as the KS cofactor****."*

- Tran et al., "*Inhalant nitrite exposure alters mouse hepatic angiogenic gene expression*.", Biochem Biophys Res Commun. **2003** Oct 17;310(2):439-45, https://www.ncbi.nlm.nih.gov/pubmed/14521929

„Inhalant nitrites are drugs of abuse that have been shown to enhance tumor growth rate in mice and are ***epidemiologically linked to an increased risk of Kaposi's sarcoma****."*

- Fung, Tran, "*Effects of inhalant nitrites on VEGF expression: a feasible link to Kaposi's sarcoma?*", J Neuroimmune Pharmacol. **2006** Sep;1(3):317-22, https://www.ncbi.nlm.nih.gov/pubmed/18040808

"In a series of studies, we showed that acute and chronic in vivo exposure to isobutyl nitrite (a representative inhalant nitrite) produced significant tissue-dependent alterations in the expression of a number of cancer- and angiogenesis-related genes in mice. In particular, hepatic mRNA and protein expression of vascular endothelial growth factor (VEGF) was significantly stimulated. The in vivo growth rate of a subcutaneous VEGF-responsive tumor was also shown to be accelerated by inhalant nitrite exposure. ***Because the development of KS is extensively linked to VEGF and its receptors, the purported link between inhalant nitrites and KS may be explained mechanistically, at least in part, through the stimulation of VEGF expression by these inhalants.****"*

Against this background, it is incomprehensible that research on nitrites (*Poppers* and *Chemsex*) is not intensified. However, Kaposi's sarcoma is very closely linked mentally to end-stage AIDS. The cause "*nitrites*" for Kaposi's sarcoma would run counter to the virus theory of AIDS. One would have to explain to the baffled patients why they are treated anti-virally (with all side effects) if the cause is the inhaled substances.

However, these form of thinking bans damages in two ways. On the one hand, by the still strong use of nitrites as *recreational drug*. On the other hand, by the antiviral treatment methods (HAART). Here, more speaks for a contribution to cancer than against it.

18.3. Nitrites, oxidative cell stress and HAART

It has long been known that nitrites lead to oxidative stress in cells, cf.

- Horne et al. "*Methemoglobinemia from sniffing butyl nitrite*.", Ann Intern Med. **1979** Sep; 91(3): 417-8, https://www.ncbi.nlm.nih.gov/pubmed/475174

- Edwards, "*Extreme methaemoglobinaemia secondary to recreational use of amyl nitrite*.", J Accid Emerg Med. **1995** Jun;12(2):138-42, https://www.ncbi.nlm.nih.gov/pubmed/7582412

In addition, nitrites in conjunction with antibiotics can convert these into toxic and carcinogenic substances, cf.

- Brambilla, "*Genotoxic effects of drug/nitrite interaction products: evidence for the need of risk assessment.*", Pharmacol Res Commun. **1985** Apr;17(4):307-21, https://www.ncbi.nlm.nih.gov/pubmed/3892549

- Brambilla, Martelli, "*Genotoxic and carcinogenic risk to humans of drug-nitrite interaction products*.", Mutat Res. **2007** Jan-Feb;635(1):17-52. Epub 2006 Dec 6, https://www.ncbi.nlm.nih.gov/pubmed/17157055

"*In an extensive search we have found that 182 drugs, representing a wide variety of chemical structures and therapeutic activities, were examined in various experimental conditions for their ability* ***to react with nitrite, and 173 (95%) of them were found to form NOC or other reactive species****. Moreover, 136 drugs were examined in short-term genotoxicity tests and/or in long-term carcinogenesis assays, either in combination with nitrite or using their nitrosation product, in order to establish whether they produce genotoxic and carcinogenic effects; 112 (82.4%) of them have been found to give at least one positive response. The problem of endogenous drug nitrosation is largely unrecognized."*

This is of particular importance, as many homosexuals who have unprotected intercourse take nitrites and in addition antibiotics to prevent venereal diseases. This was the case at least in the early years of AIDS, cf.

- Pifer et al., "*Borderline immunodeficiency in male homosexuals: is life-style contributory*?", South Med J. **1987** Jun;80(6):687-91, 697, https://www.ncbi.nlm.nih.gov/pubmed/2954211

"Results of our study suggest that white Southern male homosexuals without clinical evidence of AIDS who patronize "gay bars" may have significant zinc deficiency and moderately depressed T-helper/T-suppressor cell ratios. No single causative factor could be identified to explain the significantly low zinc and elevated copper levels measured in whole blood, as well as the depressed OKT4/OKT8 cell ratios. ***Seventy-four percent of the homosexual male subjects were "recreational" drug abusers, 81% used inhalant nitrites routinely, and 41% routinely treated themselves with antibiotics****. Eighty-one percent practiced active and/or passive penile-oral insertion, and 55.5% practiced both active and passive anal intercourse. Of the latter, 19% reported anal bleeding. Clinically inapparent, though statistically significant, borderline immunodeficiency and aberrant zinc and copper levels may be a consequence of multiple factors comprising the* ***gay bar life-style.****"*

To understand these arguments, one has to be aware that they are not starting from HIV, but from AIDS, i.e. an acquired immune deficiency (AID) and chemical causes of the with the AID syndrome associated diseases, e.g. cancer (Kaposi's sarcoma).

Cf. also

- Papadopulos-Eleopulos, "*Reappraisal of AIDS: Is the oxidation caused by the risk factors the primary cause?*", Med Hypotheses **1988**; 25:151-62, http://theperthgroup.com/SCIPAPERS/EPEMedHyp1988.pdf

"There are good reasons to doubt that HTLV-III/LAV can be regarded as the exclusive single variable in the pathogenesis of AIDS. There is therefore a spectrum of possibilities. Either it plays no role at all, is of minor significance or it contributes significantly but not exclusively to the disease. Be that as it may the one major significant variable is the ***concurrent exposure of the patients to oxidizing agents including sperm, nitrites, opiates and factor VIII****."*

As it turns out, by introducing *glutathione* as an *anti-oxidant*, replication of the putative HI virus (or what we believe is) can be prevented, cf.

- Palamara et al., "*Glutathione inhibits HIV replication by acting at late stages of the virus life cycle*.", AIDS Res Hum Retroviruses. **1996** Nov 1;12(16):1537-41, https://www.ncbi.nlm.nih.gov/pubmed/8911579

*"****We found that exogenous GSH strongly suppresses the production of p24gag protein as well as the virus infectivity. This is related to a dramatic decrease in both budding and release of virus particles from chronically infected cells (either macrophages or lymphocytes), together with a selective decrease in the expression of gp120, the major envelope glycoprotein****, rich in intrachain disulfide bonds and thus potentially sensitive to the effect of a reducing agent such as GSH. Overall data suggest that GSH can interfere with late stages of virus replication."*

Cf. also

- Kameoka et al., "*Intracellular glutathione as a possible direct blocker of HIV type 1 reverse transcription*.", AIDS Res Hum Retroviruses. **1996** Nov 20;12(17):1635-8, https://www.ncbi.nlm.nih.gov/pubmed/8947299

"In AIDS patients, chronic inflammation and elevated levels of cytokines seem to be associated with reduced levels of glutathione (GSH). GSH has been proposed to inhibit the activation of NF-kB, which results in the inhibition of HIV-1 replication. ***Here, we show the evidence that GSH and N-acetylcysteine, but not L-cysteine or dithiothreitol, could inhibit the reverse transcriptase (RT) process of HIV-1****. Such inhibition was not observed with the RT of murine leukemia virus."*

- Kalebic et al. "*Suppression of human immunodeficiency virus expression in chronically infected monocytic cells by glutathione, glutathione ester, and N-acetylcysteine*.", Proc Natl Acad Sci U S A. ***1991*** *Feb 1;88(3):986-90, https://www.ncbi.nlm.nih.gov/pubmed/1704137*

"The effects of glutathione (GSH), glutathione ester (GSE), and N-acetyl-L-cysteine (NAC) on the induction of human immunodeficiency virus (HIV) expression were investigated in the chronically infected monocytic U1 cell line, a previously described cellular model for HIV latency. U1 cells constitutively express low levels of virus, which can be increased by phorbol 12-myristate 13-acetate (PMA), tumor necrosis factor alpha (TNF-alpha), interleukin 6 (IL-6), and other inducers. ***GSH, GSE, and NAC suppressed in a dose-dependent fashion the induction of HIV expression mediated by PMA, TNF-alpha, and IL-6, in the absence of cytotoxic or cytostatic effects.****"*

"Reverse transcriptase activity, inducible by PMA, TNF-alpha, or IL-6, was decreased by 80-90% after pretreatment with GSH, GSE, or NAC. *The induction of total HIV protein synthesis was also decreased appreciably after pretreatment with GSH, GSE, or NAC. The accumulation of HIV mRNA was substantially suppressed after pretreatment with NAC but to a lesser extent after pretreatment with GSH or GSE."*

That is, the reverse transcriptase activity ***induced*** by PMA, TNF-alpha or IL-6 (activation) and which serves as a proof of a retrovirus can be reversed by glutathione (GSH), glutathione ester (GSE) or N-acetyl-L-cysteine (NAC).

Shouldn't that be top candidates for therapy purposes? Or is it rather that the reverse transcriptase activity attributed to the putative HI virus is actually an expression of oxidative cell stress that is alleviated or even eliminated by glutathione? **Then there would be little room for a virus.**

Vgl. auch zu Oxidativem Zellstress in ***aktivierten Zellen***,

- Sekkat et al., "*Oxidative phenomena are implicated in human T-cell stimulation*.", Immunology. **1988** Mar;63(3):431-7, https://www.ncbi.nlm.nih.gov/pubmed/3258279

"*Phytohaemagglutinin (PHA), phorbol myristate acetate (PMA) and PHA + PMA stimulation of T-enriched peripheral blood lymphocytes (PBL) and the Jurkat malignant T-cell line leads to oxidative-product formation,..*"

Why did nobody follow these indications in more detail? This also against the background of the severe side effects of HAART, and among others the oxidative stress induced by HAART, cf.

- Sharma, "*Oxidative stress in HIV patients receiving antiretroviral therapy*.", Curr HIV Res. **2014**;12(1):13-21, https://www.ncbi.nlm.nih.gov/pubmed/24694264

"The level of production of free radical species in HIV-1 infected individuals receiving antiretrovirals (ART) including highly active antiretroviral therapy (HAART) ***was reported to be higher than those who harbor HIV-1 infection without receiving any treatment or normal and healthy subjects****."*

- Gil et al., "*Altered oxidative stress indexes related to disease progression marker in human immunodeficiency virus infected patients with antiretroviral therapy*", Biomedicine & Aging Pathology, Vol 1 (1), Jan–Mar **2011**, p. 8-15, https://www.sciencedirect.com/science/article/pii/S2210522011000037

"The findings suggest that increased OS occurs additionally to persistent redox imbalance associated to HIV infection during apparently successfully HAART. ***This conclusion does not only underline HAART associated toxicity*** *but it may be also methodologically important for the follow-up of further clinical studies."*

- Mandas et al., "*Oxidative imbalance in HIV-1 infected patients treated with antiretroviral therapy*.", J Biomed Biotechnol. **2009**;749575, Epub 2009 Oct 26, https://www.ncbi.nlm.nih.gov/pubmed/19884983

"The study included 116 HIV-1-infected patients (86 HAART-treated and 30 untreated), and 46 HIV-negative controls. ***Serum oxidant levels were significantly higher in the HIV-1 treated group as compared to untreated and control groups. In addition, a decrease of serum total antioxidant status was observed in the HIV-1 treated group.*** *To be noted is that patients who rigorously follow antiretroviral therapy (optimal HAART adherence) have significantly higher oxidative status than those who do not closely follow the therapy (poor HAART adherence)."*

"Taken together, ***our results indicate that HAART may affect oxidative stress in HIV-1-infected patients*** *and suggest that antiretroviral therapy plays an important role in the synergy of HIV infection and oxidative stress."*

- Sundaram et al. "*Changes in antioxidant profile among HIV-infected individuals on generic highly active antiretroviral therapy in southern India*.", Int J Infect Dis. **2008** Nov;12(6):e61-6, Epub 2008 Jul 14, https://www.ncbi.nlm.nih.gov/pubmed/18621564

"At 12 months, participants on HAART showed a significant increase in glutathione peroxidase (…) and albumin (…), and a significant decrease in glutathione reductase (…) and uric acid (…) compared to baseline."

- Chandra et al. "*HIV-1 protease inhibitor induced oxidative stress suppresses glucose stimulated insulin release: protection with thymoquinone*.", Exp Biol Med (Maywood). **2009** Apr;234(4):442-53., Epub 2009 Feb 20, https://www.ncbi.nlm.nih.gov/pubmed/19234050

"However, long-term exposure to HAART is associated with a metabolic syndrome manifesting cardiovascular dysfunction, lipodystrophy, and insulin resistance syndrome (IRS). The inclusion of HIV-1 protease inhibitors (PIs) in HAART has been linked to the induction of IRS."

"The present study showed that exposure to several different PIs, nelfinavir (5-10 microM), saquinavir (5-10 microM) and atazanavir (8-20 microM), decreases glucose stimulated insulin secretion from rat pancreatic beta-cells (INS-1). ***Nelfinavir significantly increased reactive oxygen species (ROS) generation and suppressed cytosolic****, but not mitochondrial superoxide dismutase (SOD) levels. Nelfinvair also decreased both glutathione and ATP and increased UCP2 levels in these cells."*

- Honnapurmath et al., "*Antiretroviral Therapy-induced Insulin Resistance and Oxidative Deoxy Nucleic Acid Damage in Human Immunodeficiency Virus-1 Patients*.", Indian J Endocrinol Metab. **2017**, Mar-Apr;21(2):316-321, https://www.ncbi.nlm.nih.gov/pubmed/28459032

"In this study, we observed that ***ART plays a significant role in the development of IR and oxidative DNA damage*** *in HIV-positive patients taking ART."*

- Kolgiri et al., "*Association of Metabolic Syndrome and Oxidative DNA Damage in HIV/AIDS Patients*.", Indian J Clin Biochem. **2018** Jul;33(3):273-281, https://www.ncbi.nlm.nih.gov/pubmed/30072826

"MS and oxidative DNA damage were significantly higher in HIV-positive patients with second line ART and first line ART than ART-naive patients*. In a logistic regression analysis, increased MS was positively associated with the increased DNA damage (OR: 29.68, 95%:13.47, CI: 65.40) P = 0.0001.* ***ART plays a significant role in the development of MS and oxidative DNA damage in HIV-positive patients taking antiretroviral therapy****."*

- Smith et al, "*Beyond the polymerase-γ theory: Production of ROS as a mode of NRTI-induced mitochondrial toxicity*", PLoSONE 12(11):e0187424, Nov 2, **2017**, https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0187424

"Many NRTI induced adverse events have been linked to the incurrence of oxidative stress, although the causality of events leading to reactive oxygen species (ROS) production and their role in toxicity is unclear. In this study we show that short-term effects of first generation NRTIs, which are rarely discussed in the literature, include ***inhibition of oxygen consumption, decreased ATP levels and increased ROS production****."*

- Caron et al., "Contribution of mitochondrial dysfunction and oxidative stress to cellular premature senescence induced by antiretroviral thymidine analogues.", Antivir Ther. 2008;13(1):27-38, https://www.ncbi.nlm.nih.gov/pubmed/18389896

"Mitochondrial changes and oxidative damage could partly explain the premature senescence of fibroblasts and adipose cells induced by stavudine andzidovudine. This suggests that thymidine analogues might be involved in the early aging-related diseases observed in some HIV-infected patients taking antiretroviral drugs."

How do you want to distinguish the effects of a suspected virus from the effects of the so-called medications? And furthermore, how does one differentiate the effect of other oxidative substances in risk groups? How much space is left for an infectious virus?

19. Transfer rates in heterosexual couples

For years, people have been trying to translate AIDS from high-risk groups into the heterosexual sector and to promote prophylaxis there to serodiscordant couples (i.e., one partner HIV- and one partner HIV+).

This corresponds by no means to the original population in which the later called *AIDS-defining diseases* were first detected. In view of the above findings, there are considerable doubts about this procedure. This is probably the attempt to normalize a clearly asymmetric epidemic. At the same time you can sell tests and prophylaxis.

The doubts are appropriate, because the transmission rates in serodiscordant, heterosexual couples are very low, about 1 in 1000 sexual contacts, cf.

- Duesberg, Schwartz, "*Latent Viruses and Mutated Oncogenes: No Evidence for Pathogeni*city", Progress In Nucleic Acid Research and Molecular Biologi, Vol. 43 , **1992**, p. 135 -204, https://www.ncbi.nlm.nih.gov/pubmed/1410445

"*Sex is another, although highly inefficient, mode of transmission, depending on an average of over 1000 sexual contacts*."

And this means 1000 unprotected contacts. Precisely because of the extremely low prevalence (frequency) of HIV in women, a self-test is therefore strongly discouraged. The positive predictive value of the tests (see also below, Annex I) is <1%, i.e. from 100 positive HIV self-test results, on average less than 1 is really positive. And that without it being clear what the pathogenic consequence of the test is.

Cf. also

- Hughes et al., "*Determinants of per-coital-act HIV-1 infectivity among African HIV-1-serodiscordant couples.*", J Infect Dis. **2012** Feb 1;205(3):358-65, https://www.ncbi.nlm.nih.gov/pubmed/22241800

"*In this prospective study of 3297 African HIV-1 discordant couples, we found unadjusted* ***per-act risks of unprotected MTF and FTM transmission of 0.0019 and 0.001****, respectively*."

- Boily et al., "Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies.", Lancet Infect Dis. **2009** Feb;9(2):118-29, https://www.ncbi.nlm.nih.gov/pubmed/19179227

"*We conducted a systematic review and meta-analysis of observational studies of the* ***risk of HIV-1 transmission per heterosexual contact.*** *The search to September 2008 identified 43 publications based on 25 different study populations.* ***Pooled female-to-male (0·0004, 95% CI=0·0001-0·0014) and male-to-female (0·0008, CI=0·0006-0·0011)*** *transmission estimates in developed countries reflected a low risk of infection in the absence of antiretroviral*"

It is also very strange that HIV infections of women should not depend on the sexual practice, that is quite different than with homosexual men, cf.

- Lawrence et al. "*Human immunodeficiency virus transmission from hemophilic men to their heterosexual partners*", **1991** Oct 16, In: Heterosexual transmission of AIDS: Alexander, N.J., Gabelnick, H.L. and Spieler, J.M. (Eds) Wiley-Liss, New York, 1990, https://www.popline.org/node/369968

"*The HIV seropositivity among the female partners **did not correlate significantly** with the frequency of sexual intercourse, condom use, history of sexually transmitted diseases or anal intercourse."*

Cf. also

- Padian et al. "*Heterosexual transmission of human immunodeficiency virus (HIV) in northern California: results from a ten-year study.*", Am J Epidemiol. **1997** Aug 15;146(4):350-7, https://www.ncbi.nlm.nih.gov/pubmed/9270414

*"We followed 175 HIV-discordant couples over time, for a total of approximately 282 couple-years of follow-up (table 3). Because of deaths as well as the break-up of couples, attrition was severe; only 175 couples are represented in table 3. The longest duration of follow-up was 12 visits (6 years). **We observed no seroconversions after entry into the study.**"*

*"**No transmission** occurred among the 25 percent of couples who did not use condoms consistently at their last follow-up nor among the 47 couples who intermittently **practiced unsafe sex during the entire duration of follow-up.**"*

That's really little: **no transmission in 6 years**.

This study (Padian) is of particular importance, as it includes data from serodiscordant heterosexual couples ***until*** 1996. HAART was introduced in 1996. However, this study shows the same low, sometimes lower, transmission rates than later studies that included HAART-treated humans. This clearly speaks against the efficacy of HAART in preventing transmission in heterosexual couples. But it is the same pattern as always: we see no effect (here: no transmission), so HAART is effective.

Contrary to the claim, breastfeeding does not affect infant mortality in HIV+ measured mothers, cf..

- Kagaayi et al., "*Survival of infants born to HIV-positive mothers, by feeding modality, in Rakai, Uganda.*", PLoS One. **2008**;3(12):e3877, https://www.ncbi.nlm.nih.gov/pubmed/19065270

"*One hundred eighty two infants born to HIV-positive mothers were followed at one, six and twelve months postpartum. Mothers were given infant-feeding counseling and allowed to make informed choices as to whether to formula-feed or breast-feed. […] **The cumulative 12-month probability of infant mortality was 18% among the formula-fed compared to 3% among the breast-fed infants.**"*

*"**Formula-feeding was associated with a higher risk of infant mortality than breastfeeding in this rural population.**"*

There have been cases in which the children of HIV+ measured mothers have been taken away because the mothers continued to breastfeed their own children. A reference to this publication may be helpful in a trial.

The low transfer rates in the heterosexual area continue in the area of female prostitution. In the meantime *HIV-1 resistance* of sex workers is being talked about, cf.

- Burgener et al. "*Identification of differentially expressed proteins in the cervical mucosa of HIV-1-resistant sex workers*.", J Proteome Res. **2008** Oct;7(10):4446-54, https://www.ncbi.nlm.nih.gov/pubmed/18707157

"*Novel tools are necessary to understand mechanisms of altered susceptibility to HIV-1 infection in women of the Pumwani Sex Worker cohort, Kenya.* ***In this cohort, more than 140 of the 2000 participants have been characterized to be relatively resistant to HIV-1 infection****."*

Science does not really have an explanation for this. But a lot of protein analysis without any reference to the suspected, classical infections by sexually transmitted diseases. It remains guesswork on a high level.

The low transmission rates in heterosexual couples are also reflected from the beginning on in the statistics on infection of female prostitutes. Within non-drug-dependent, female prostitutes this does simply not take place, cf.

- Rosenberg, "*Prostitutes and AIDS: a health department priority*?", Am J Public Health. **1988** Apr;78(4):418-23, https://www.ncbi.nlm.nih.gov/pubmed/3279838

"However, a variety of studies suggest that human immunodeficiency virus (HIV) infection in prostitutes follows a different pattern than that for STDs: ***HIV infection in non-drug using prostitutes tends to be low or absent,*** *implying that sexual activity alone does not place them at high risk,* ***while prostitutes who use intravenous drugs are far more likely to be infected with HIV****."*

"*Other prostitute studies tend to be small but similarly emphasize the central role of drug use as a major risk factor: in New York City, 50 per cent of 12 drug users were positive, compared with 7 per cent of 65 nonusers;* ***in Italy, 59 per cent of 22 drug users were positive, whereas none of the nonusers were****.* ***None of the 50 prostitutes tested in London, 56 in Paris, or 399 in Nuremberg were seropositive. The disparity in rates according to drug use suggests that drug use may overshadow sexual exposure as a risk factor among these women****. In parts of Africa, however, infection rates are high among female prostitutes and appear to be related only to sexual activity. However, there may be other relevant factors which affect susceptibility in that population."*

20. LTNP – Long Term Non Progressors

According to the literature it takes an average of 10 years for the symptoms of AIDS-defining diseases to show, cf.

- *Fauci et al. "Immunopathogenic* Mechanisms of HIV Infection", Ann Intern Med. **1996**; 124(7), p. 654-663, http://annals.org/aim/fullarticle/709558/immunopathogenic-mechanisms-hiv-infection

"*The duration of clinical latency varies, but progression to the acquired immunodeficiency syndrome typically occurs* ***after a mean of approximately 10 years****."*

Unless you are a long-term non-progressor (LTNP). Then it can take any time. This is known since longtime and is also unrelated to the completely useless CD4 cell count, especially in the multiple infected and strongly drug-dependent population on which the HIV=AIDS theory had been developed.

- Hoover et al., "*Long-term survival without clinical AIDS after CD4+ cell counts fall below 200 x 10(6)/l.*", AIDS. **1995** Feb;9(2):145-52, https://www.ncbi.nlm.nih.gov/pubmed/7718184

"Although antiretroviral therapy and Pneumocystis carinii prophylaxis extend AIDS-free survival, ***45% of the group who were AIDS-free > or = 3 years after CD4+ cells fell below 200 x 10(6)/l had not used these treatments.****"*

"CONCLUSIONS:

Significant numbers of individuals remain free of illnesses and AIDS symptoms > or = 3 years *after CD4+ cell counts drop below 200 x 10(6)/l.* ***This occurs even in the absence of treatment****. The associations seen here suggest that host and viral factors play important roles."*

As we have learned above this result from 1995 result would not have persist today. As stated above, the CD4 cell number, as useless as it is, has replaced the AIDS diagnosis. By the actual definition these people would not be AIDS-free because of their CD4 cell counts.

Andy Reiss and Joan Shenton's film "*Positive Hell*" from 2014 features LTNPs, some of whom have been living with an HIV+ diagnosis for 30 years without ever having taken medication such as HAART.

- Reiss und Shenton, „*Positive Hell*" (**2014**), http://www.positivehell.com/story/

"*Some of them, like physician Dr Manuel Garrido,* ***have never taken any antiviral drugs****. He's been swimming against the tide of medical orthodoxy* ***for three decades****."*

There is not only AIDS without HIV. These are all those who "*classically*" fall ill with an AIDS-defining illness. There is also HIV without AIDS. This violates Koch's postulates for the presence of an infectious agent.

- Sivay et al., "*Natural control of HIV infection in young women in South Africa: HPTN 068*", HIV Clin Trials. **2018** Oct;19(5):202-208, https://www.ncbi.nlm.nih.gov/pubmed/30522410

*"**In this cohort, 5.6% of women who were not using ARV drugs had sustained viral suppression**. This represents a minimum estimate of the frequency of viremic controllers in this cohort, since some women were not followed long enough to meet the criteria for classification."*

5.6% of women are infected, but show no symptoms. That's a bit much for a spontaneous healing.

Depending on the publication, the prevalence of LTNP is up to 22%. The values vary according to the study, cf.

- Sabin, Lundgren, "*The natural history of HIV infection*", Current Opinion in HIV and AIDS: July **2013**, Vol 8(4), p. 311–317, https://journals.lww.com/co-hivandaids/fulltext/2013/07000/The_natural_history_of_HIV_infection.10.aspx

From this publication table 1:

Table 1. Definitions of long-term nonprogressors used in recent studies

Author (reference)	Symptoms allowed	ART allowed	Period of follow-up	CD4 requirement	Additional requirements/comments	Reported prevalence
Madec *et al.* [3]	Asymptomatic	No ART	>8 years after first positive HIV test	All ≥500 cells/μl	Study includes a high proportion of known seroconverters	9.0%
Okulicz *et al.* [4]	No AIDS	No ART	>7 years after diagnosis	All ≥500 cells/μl	–	5.0%
	No AIDS	No ART	>10 years after diagnosis	All ≥500 cells/μl	–	2.0%
Grabar *et al.* [5]	Asymptomatic	No ART	>8 years after diagnosis	Nadir >500 cells/μl	At least three CD4 and HIV RNA assessments available in 5 years prior to 2005	22.3%
	Asymptomatic	No ART	>8 years after diagnosis	Nadir >600 cells/μl	As above	11.4%
	Asymptomatic	No ART	>8 years after diagnosis	Nadir >600 cells/μl	As above, and positive CD4 slope over 5 years prior to 2005	2.8%
Mandalia *et al.* [6▪▪]	Asymptomatic	No ART	>7 years after diagnosis	>450 cells/μl	Stable CD4 slope (≥0 cells/μl per year) over entire follow-up period	0.2%
Gaardbo *et al.* [7]	Not stated	No ART	>10 years after diagnosis	>350 cells/μl	Viral load >5000 copies/ml	*N* = 14, prevalence not stated
Ballana *et al.* [8]	Not stated	No ART	>10 years after diagnosis	All >500 cells/μl	Viral load <10000 copies/ml	*N* = 155, prevalence not stated

ART, antiretroviral therapy.

(*from Sabin, Lundgren, "The natural history of HIV infection", **2013***)

There is some evidence that the true number of LTNPs is higher than stated here:

a) Some people do not even know that they are HIV+. They just keep on living. These cases are not recorded.

b) In addition, the diagnosis is made by the CD4 cell count or the HIV RNA virus count (PCR), despite of all problems with these measurement methods. These people continue to show no symptoms, so they are actually still LTNP, but due to measured values (CD4 cell count) are defined as sick and fall out of the LTNP statistics.

c) **The criteria for LTNP are partly designed so that even the healthiest person cannot fulfill them**: the slope of the CD4 curve ("*stable CD4 slope*") must never be negative (always ≥ 0). That means, a flu-like infection in the study, which leads to a transient decrease in the CD4 number, and no more LTNP.

The number of LTNP is held artificially small. This is important because HIV+ without AIDS in 22% and more cases means a blatant violation of Koch's postulates.

And there is an additional problem:

d) The maxim "*hit hard and early*" blurs the line between LTNP and patients with AIDS-defining diseases. By the fact that people start HIV treatment very early on without it being clear that they will ever show symptoms of immunodeficiency many possible LTNP are being treated and thus are falling out of the LTNP statistic ("*No ART*").

At the same time, it should not be overlooked that these people are told by (almost) the entire current scientific community that they are actually ill and will soon show the symptoms of a deadly disease, e.g. Diarrhea or prolonged fever, see above. That means the investigated population is under extreme negative stress and not everyone will be able to cope with this situation (see above for the suicide numbers).

21. AIDS and Africa

That AIDS allegedly is rampant in Africa has gone through the media many times. Authors of such campaigns is among others the WHO or UNAIDS. It remains unclear whether people there show clinical symptoms, what proportion is based on questionable measurements and what proportion is simply estimated.

Particularly in the case of AIDS deaths, great caution is required in Africa, since in most countries there is no reporting system and the data is estimated.

In addition, it is often overlooked in the media that there are a whole range of other causes of death that are hard to be differentiated from AIDS-defining diseases, e.g. diarrhea, prolonged fever or weight loss, e.g. while starving.

In particular, the children in Africa, mentioned by UNAIDS in 2018 may have been measured HIV+ (HIV-1 or HIV-2). But they will not get AIDS unless their immune system is weakened by malnutrition, heavy metals in the water, parasites, malaria, typhoid or tuberculosis and / or drugs.

In this regard, HIV / AIDS hysteria obscures actual disasters in developing countries. It leads to such absurdities that $ 10 million from the WHO are available for HIV prevention, but not $ 1,000 to protect a water hole against animal feces (parasites). Cf.

- Geshekter, "*Myths and Misconceptions of the Orthodox View of AIDS in Africa*", Etica & Politica / Ethics & Politics, IX, **2007**, 2, pp. 330-370, https://www.openstarts.units.it/bitstream/10077/5283/1/Geshekter_E%26P_IX_2007_2.pdf

"*Apartheid policies ignored the diseases that primarily afflicted Africans - malaria, tuberculosis, respiratory infections and protein anemia. Even after the end of apartheid, the absence of basic sanitation and clean water supplies still affects many Africans in the former homelands and townships. The article argues that the billions of dollars squandered on fighting AIDS should be diverted to poverty relief, job creation,* ***the provision of better sanitation, better drinking water****, and financial help for drought-stricken farmers.* ***The cure for AIDS in Africa is as near at hand as an alternative explanation for what is making Africans sick in the first place.***"

"*For instance, a 1994 study in central Africa reported that the microbes responsible for tuberculosis and leprosy were so prevalent* ***that over 70% of the HIV-positive test results were false****. The study also showed that* ***HIV antibody tests register positive in HIV-free people whose immune systems are compromised for a variety of reasons, including chronic parasitic infections and anemia brought on by malaria*** *that are widespread in populations with the diseases of poverty.*"

- Neville Hodgkinson, "*Aids sunset gives way to new dawn in Uganda*", The Business, 19/20 October **2003**, https://barnesworld.blogs.com/Uganda.pdf

"Fiala asks: 'How can this contradiction be explained: that a land condemned to death has not only avoided the predicted catastrophe but that population growth has even dramatically accelerated in this period and economic development has been positive? And more specifically: ***how has it been possible to reduce HIV-prevalence without antiretroviral therapy, the so-called Aids drugs?****'"*

"In estimating total Aids cases, until recently WHO's Geneva headquarters added the registered Aids sufferers to a high number of unreported cases which WHO presumedto have occurred. Thus in November 1997, WHO announced that since its previous report in July 1996, there had been a further 4.5m Aids cases in

*Africa. In this period, however, only 120,000 Aids sufferers were actually registered. "**In other words, 97% of the supposed new Aids cases occurred only at the WHO HQ in Geneva**," Fiala comments."*

*"In Uganda, there were 4,000 aid organisations in 1994 active in the fight against HIV/Aids; yet many people still have no access to clean drinking water, Fiala found. "In 1990 the figure was 56 % [with clean water]. Ten years and millions of dollars later, it was 50%." In Kyotera, a town in the Rakai district, a particularly large amount of money had been spent on Aids, because it was supposed to be the most heavily affected. "Despite millions of aid funds, campaigns for abstinence and the distribution of condoms, **the people of Kyotera still have to get their water during most of the year from an unprotected water hole which they share with cattle.**"*

- Papadopulos-Eleopulos et al., "*AIDS in Africa: distinguishing fact and fiction*", World J Microbiol Biotechnol. **1995** Mar;11(2):135-43, https://www.ncbi.nlm.nih.gov/pubmed/24414488

*"**Seropositivity to HIV in Africans usually represents no more than cross-reactivity caused by an abundance of antibodies induced by the numerous infectious and parasitic diseases which are endemic in Africa**. The apparently high prevalence of 'AIDS' and 'HIV' seropositives is therefore not surprising and is not proof of heterosexual transmission of either HIV or AIDS."*

- Mwizenge Sani Tembo, "*The Deadly Fallacy of the HIV-AIDS-Death Hypothesis: Exposing the Epidemic that Is Not*", 12/13/**04** revised 01/29/**14**, https://wp.bridgewater.edu/mtembo/articles/hiv-aids-scientific-controversy/

"No !!! yamene AIDS na malaria yavuta. Sure imwe munthu akadwala malaria basi mwaziba azankhala positive ku AIDS. Bati imwe!! I don't believe mwe.

*"No!! this AIDS disease and malaria are very troublesome. **How come that if someone becomes sick with malaria fever they automatically become positive for AIDS?** How is this possible!? This is incredulous!"*

*This is the closest translation into English of what she had said in Lusaka Nyanja lingua franca. The translation, however, does not reflect her incredulous tone, that also reflected her astoundment, befuddlement, helplessness, and skepticism. She was asking: **'how was it that nearly everyone who was coming down with malaria was automatically also found positive for HIV?!!'**"*

- Lawn et al., "*Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa*", AIDS. **2008** Oct 1; 22(15): 10.1097, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3816249/

*"Immunological and virological responses to ART are similar to responses in patients treated in high-income countries. **Despite this, however, early mortality rates in sub-Saharan Africa are very high; between 8 and 26% of patients die in the first year of antiretroviral treatment, with most deaths occurring in the first few months.** […] Although data are limited, leading causes of death appear to be tuberculosis, acute sepsis, cryptococcal meningitis, malignancy and wasting syndrome. Mortality rates are likely to depend not only on the care delivered by antiretroviral treatment programmes, but more fundamentally on how advanced disease is at programme enrolment and the **quality of preceding healthcare."***

Is it the general condition of the health service or the (missing) nutrition?

Even against this background, one could not blame the people there if they were quite open-minded to the HI virus. It is unclear to what extent possible disincentives, e.g. through accompanying medical examinations or meals during a HAART therapy, play a role in statistics.

It is also often overlooked that HIV / AIDS is also an instrument of power that not only excludes homosexuals. It is possible to construct almost arbitrary correlations with suspected and assumed codes of conduct in ethnic groups, cf.

- Zacharias et al. "High false-positive rate of human immunodeficiency virus rapid serum screening in a **predominantly hispanic prenatal population**.", J Perinatol. **2004** Dec;24(12):743-7, https://www.ncbi.nlm.nih.gov/pubmed/15318249

"*The positive predictive value of rapid HIV-ELISA* ***during pregnancy varies widely, depending on maternal race/ethnicity and sexual behavior.*** *The routine disclosure of rapid intrapartum HIV serum screening results prior to Western blot confirmation should be avoided in very low-risk populations."*

That is strange. It is, however, quite in line with the US American pattern of thinking regarding South American immigrants. Any sexual behavior is assumed to belong to ethnic minorities.

On the opposite case cf.

- Smith et al. "*Ethnicity and discordance in plasma HIV-1 RNA viral load and CD4+ lymphocyte count in a cohort of HIV-1-infected individuals.*", J Clin Virol. **2003** Jan;26(1):101-7, https://www.ncbi.nlm.nih.gov/pubmed/12589840

"These results suggest that plasma HIV-1 VL is ***discordantly low in Black compared with Caucasian*** *groups stratified for CD4+ count, in this cohort of antiretroviral naive HIV-1-positive individuals living in London."*

That's the situation in 2 clinics in East London. Conversely to the situation in Africa. How come? How reliable are these statistics?

That there are many things wrong in Africa is also shown by the increasing indications that the numbers that are coming from there are far too high. Cf.

- John Donnelly, June 20, **2004**, "*Estimates on HIV called too high - New data cut rates for many nations*"; http://archive.boston.com/news/world/articles/2004/06/20/estimates_on_hiv_called_too_high/

"Estimates of the number of people with ***the AIDS virus have been dramatically overstated in many countries*** *because of errors in statistical models and a possible undetected decline in the pandemic, according to new data and specialists on the disease."*

"*In many nations, analysts are cutting the estimates of HIV prevalence by half or more."*

"And the numbers in India are coming under increasing scrutiny because surveys in ***AIDS hot spots are indicating a prevalence rate that is much lower than the national average****."*

"*Already, earlier this year, US officials told Rwandan AIDS administrators that if HIV prevalence estimates* ***were to drop to 5 percent, the country's AIDS funding may be cut,*** *according to both US and Rwandan officials, speaking on condition of anonymity."*

Is it all about keeping the countless organizations alive with a supposed epidemic, and therefore producing new horror numbers each year?

It seems that way. The role of the multinational organization is increasingly being questioned, cf.

- Roger England, „*The writing is on the wall for UNAIDS*", BMJ **2008**; 336, https://www.bmj.com/content/336/7652/1072.full

"*HIV exceptionalism is dead—and the writing is on the wall for UNAIDS. Why a UN agency for HIV and not for pneumonia or diabetes, which both kill more people?*"

"Putting HIV in its place among other priorities will be resisted strongly. ***The global HIV industry is too big and out of control****. We have created a monster with too many vested interests and reputations at stake, too many single issue NGOs (in Mozambique, 100 NGOs are devoted to HIV for every one concerned with maternal and child health), too many relatively well paid HIV staff in affected countries, and too many* ***rock stars with AIDS support as a fashion accessory."***

21.1. Remarks on *Chigwedere et al.*

It is now time to address the model calculations of Chigwedere et al. and to evaluate this much-cited, alleged evidence that the so-called *AIDS denialism* cost between 2000 and 2005 about 330,000 lives. This is opportune because, after all, we are talking here about the *Harvard School of Public Health* and the elite of medical research, cf.

- Chigwedere et al., "*Estimating the lost benefits of antiretroviral drug use in South Africa*.", J Acquir Immune Defic Syndr. **2008** Dec 1;49(4):410-5, https://www.ncbi.nlm.nih.gov/pubmed/19186354

It's not the only ***model calculation*** of this kind, it's easy to find more. All have in common that the blessing would be in the medication and the *blessed* HAART alone.

The starting point is marked by the abnormality that the HIV prevalence in South Africa, in contrast to the US, Europe and also large parts of Asia (including China), see Appendix I, instead of 1: 1.000 (risk groups) and 1: 10.000 (Non-risk groups), amounts to 1: 5 to 1:10. Thus, a factor of 100 - 200 (risk groups) or 1.000 – 2.000 (non-risk groups) higher. Almost exclusively affected is the black population. Cf.

- UNAIDS DATA 2018, http://www.unaids.org/sites/default/files/media_asset/unaids-data-2018_en.pdf

As of 2017

Country	People living with HIV (all ages)	Total population	Prevalence
South Africa	7.200.000	56.521.900	**13%**
Germany	91.000	83.000.000	**0,1%**

At the same time, the ***proportion of HIV+ measured women is> 50%***, cf.

- Hansoti et al, *„A Window Into the HIV Epidemic from a South African Emergency Department*.", AIDS Res Hum Retroviruses. **2019** Feb; 35(2):139-144, https://www.ncbi.nlm.nih.gov/pubmed/30215268

„The study was conducted between September and November 2016 at the Frere Hospital Emergency Department in East London, South Africa. ***The overall HIV prevalence in our study population was 26.9%*** *[...].* ***The highest prevalence was observed among females in the 30-39 years age group [60.3% (…)]. HIV prevalence was significantly higher among females compared with males*** *in both the 20-29 years age group and 30-39 years age group (p < .05), but nearly identical to older age groups."*

In contrast to the industrialized countries where the suspected HI virus spreads from the beginning until today almost exclusively (> 90%) in homosexual men (MSM - Men having sex with men), see Annexes I and III.

It should also be noted that we speak almost exclusively of the ***black population in South Africa***.

Chigwedere et al. do not address these abnormalities and the widely differing modes of distribution of the suspected HI virus in industrialized countries and Africa, or even compared to Asia. Instead, one estimates lives that HAART could have allegedly saved, cf. Chigwedere et al., ibid,

"To estimate the lost benefits of ARV drug use in South Africa, we compared the actual number of persons who received ARVs for treatment or PMTCT between 2000 and 2005 with what was reasonably feasible in the country during that period. ***The difference, multiplied by the average efficacy of ARV treatment or PMTCT prophylaxis gives us the lost benefits of ARV use****."*

The problem is that there is no evidence for the alleged efficacy of HAART as a lifelong(!) therapy. ***I.e. the multiplicative factor of the mean AVR efficacy is = 0.*** With these drugs, no lives are saved, cf. chapter 4 - *Current HIV therapy approaches and their consequences*. The same holds true for the alleged mother-to-child prophylaxis, cf. chapter 4.1 - *HAART and pregnancy or children*.

There are numerous side effects (see above), which correspond to 100% of the alleged clinical pictures. ***HAART has never healed any person from the AID syndrome***. Instead, people under HAART die slowly but steadily. Nowadays, they are dying more slowly than they used to, as drug doses are lower. In Chigwedere et al. speaks the pharmaceutical industry, which pats itself on the back.

In addition to the severe and finally fatal side effects of HAART, Chigwedere et al. also ignore how many lives could have been saved if the money had been invested in clean water, nutrition and classical medical infrastructure instead of HIV focus labs, as President Thabo Mbeki reminded at that time, cf.

- Lizeka Tandwa, News24, "*Mbeki was right about HIV and Aids*", **2016**-03-10, https://www.news24.com/SouthAfrica/News/mbeki-was-right-about-hiv-and-aids-researchers-20160310

"Brink said the outrage at Mbeki's stance on HIV came from white liberal establishments who had bought a story sold by America. "The outrage comes from the people who are our 'friends'. These are the white liberalist establishment, the principally colonised and Christian Africans who bought the story from America." he said."

and

- Thabo Mbeki, Mail & Guardian, "*Mbeki addresses 'Aids denialism' criticism*", 07 Mar **2016**, https://mg.co.za/article/2016-03-07-a-brief-commentary-on-the-question-of-hiv-and-aids

"During the same year, October 1985, German researchers had an article published in the British medical journal, The Lancet. They stated that: "The data suggest that HTLV-III was rare in Africa until recently, and still is rare in much of the continent."

***Some of our friends, the friends of the Africans, say that five years later, this situation had changed completely**. They say that now, in our region and country, the HI Virus was transmitted heterosexually and that it had become endemic."*

"To all intents and purposes, 15 years later, this situation has not changed both in the US and in Western Europe. But, as we have said, and as is generally known, our own situation has changed radically, resulting also in it being said that we now have the highest incidence of HIV or the spread of HIV in the world.

*The question that arises from this is – why! **Why does the same Virus behave differently in the US and Western Europe from the way it behaves in Southern Africa**!"*

*"**Why did it come about that so much noise was made internationally about the 9th leading cause of death in our country, with not even so much as a whimper about the 1st leading cause of death, tuberculosis?***

Why would the South African Government, knowing the health condition of its own population very well, have been expected so to focus on the 9th leading cause of death as virtually to treat as less urgent and important the first eight (8) leading causes of death, even taken together?

Did this have to do with the fact that South Africa could be a lucrative market for the sale of ARVs, as it now is?"

*"**Poverty is the main reason why babies are not vaccinated, why clean water and sanitation are not provided, why curative drugs and other treatments are unavailable and why mothers die in childbirth**. It is the underlying cause of reduced life expectancy, handicap, disability and starvation.*

Poverty is a major contributor to mental illness, stress, suicide, family disintegration and substance abuse. Every year in the developing world 12.2 million children under 5 years die, most of them from causes which could be prevented for just a few US cents per child. They die largely because of world indifference, but most of all they die because they are poor."

Of all this, we read nothing at Chigwedere et al., the Harvard experts. Only antiviral medicine saves South Africa? No. People are dying all over Africa, as always, among others, from poverty, malnutrition, dirty drugs, heavy metals in drinking water, classical infections, e.g. malaria and tuberculosis, or parasites.

Because President Mbeki has pointed out the obvious, the term ***AIDS denialism*** has been coined. In addition, within 10 years the alleged prevalence of HIV has risen from 0% to> 50%. With the effect that now all other causes of death can be ignored? Instead, billions in sales of antiviral therapies are generated. For these people, one should coin the term ***Poverty Denialism***.

Given the many false-positive serological tests in otherwise stressed bodies (by the factors mentioned), the estimated prevalence figures used in Chigwedere et al. must also be strongly doubted.

Since almost exclusively the black population in South Africa (and neighboring countries such as Botswana or Namibia) is affected, one must also ask to what extent ***HIV=AIDS*** is the ***instrument of power*** of a white minority, sponsored by Harvard University.

22. HIV in trials - acquittal in a murder trial thanks to HIV

Is there anything that cannot be explained with HIV and HIV-related diseases? Not according to the experts.

The case is not without controversy, including among others the skin color of the defendant and the general treatment of rape victims. However, for the defense, the statement of a so-called *HIV expert* was of decisive importance, cf.

- RNZ, "*HIV expert gives evidence in Gwaze trial*", 18 May **2012**, https://www.radionz.co.nz/news/national/106053/hiv-expert-gives-evidence-in-gwaze-trial

*"Crown counsel says the **10-year-old was killed after her air supply was interrupted** by the holding of a hand or pillow across her mouth and that she suffered a severe sexual attack."*

*"**Professor Lucas**, a histologist with expertise in HIV, said the **anal injuries** the Crown maintains she received during a sexual attack were also caused by her condition.*

*His conclusion is that the **shortage of oxygen to the brain** that lead to Miss Makaza's death was the result of toxic shock which stemmed from her HIV infection."*

- NZ Herald, " *Gwaze's DNA found on niece's clothing and sheets*", 21 May, **2012**, https://www.nzherald.co.nz/nz/news/article.cfm?c_id=1&objectid=10807396

"*Two other pairs of her underpants, as well as a skirt she was wearing the night she died, also showed traces of the murder accused's DNA.*

But the defence witness agreed with Gwaze's lawyer Jonathan Eaton that in a house with a "sexually active male" there was a "very real possibility" that underpants semen stains will transfer during the household's washing cycles, either by hand-wash or machine-wash."

- Martinique Stilwell, "*Who killed Charlene Makaza?*", 01 Mar **2013**, https://mg.co.za/article/2013-02-01-00-who-killed-charlene-makaza

*"When she was five months old, **Charlene's mother died of tuberculosis (TB)** and Sifiso adopted Charlene and her older sister, Charmaine. The girls' biological father died two years later."*

"However, Charlene never received ARVs…"

*"Martin Sage, the Crown pathologist in Christchurch, performed the autopsy. **He described a well-nourished child with fresh bruising of her arms**. Notes were made of severe brain damage consistent with hypoxia, or lack of oxygen, and **several bloody anal lacerations, bruising of the vulva and a fresh hymenal tear.**"*

*"He [Lucas] said HIV itself could cause the breakdown and bleeding of her anus and vulva. Although **he was unable to cite a single publication showing HIV causing such breakdown in children**, he had **heard of** anal changes in HIV-positive adults and could see no reason why children could not suffer the same condition.*

*Brian Eley, professor of infectious diseases at Red Cross Children's Hospital and a member of the WHO panel for paediatric HIV, submitted a report stating that **Charlene's ano-genital findings were not consistent with HIV infection**."*

There is probably nothing, according to the "*experts*" for which the suspected HI virus cannot be responsible. If Dr. Lucas is believed, cf.

- Lucas, Nelson, „*HIV and the spectrum of human disease.*", J Pathol. **2015** Jan;235(2):229-41, https://www.ncbi.nlm.nih.gov/pubmed/25251832

"Third, through immune activation and effects on endothelia, it can cause more subtle systemic organ damage, such as chronic ***cardiovascular, hepatic, pulmonary*** *and* ***central nervous system disease****."*

Very strange that these are exactly the observed side effects of HAART, see above.

HIV does not cause bruises on the arms. And no lacerations in the anal or vaginal region. For decades, the side effects of HAART have been attributed to the putative HI virus. This is then sold as a diagnosis. But the 10-year-old *Charlene Makaza* did not take any HAART medication. So what is the explanation for the bruises and the lacerations?

Plausible seems rather that here a child molester and child murderer has gone unpunished. Thanks to HIV and a so-called *HIV expert*.

It is an integral part of the HIV / AIDS discussion to push the obvious aside, e.g. the extremely high correlation of drugs and classical infections with AIDS, and instead experts are speculating on HIV, for which they cannot give a single reference. They simply rely on the broad, scientific consensus on HIV.

In a jury trial under New Zealand law, the verdict may be "*in doubt for the accused*". How should jurors, i.e. normal citizens, who are not directly aware of the essential connections, judge differently? What should citizen do but trust in the *consensus of science*?

We continue to read the data so that in case of doubt it has always been the putative HI virus. That is not very scientific. And it is not just.

23. (~~How~~) Does HIV-1 cause AIDS?

Some things are just too good to be true. HIV (not AIDS!) is still a huge money printing machine.

Who wants to give that up?

Everything is based on the assumption that HIV is the infectious and transmissible cause of AIDS. But is that so?

I don't think so.

Shortly after the announcement by Heckler and Gallo in 1984 that HIV is the cause of AIDS, practically all experiments that sought to test alternative causes have come to a halt, and doubters have been neutralized, see above. This makes an absolute proof difficult.

Despite considerable doubts, e.g. due to the bystander cell problem, there is no research that studies co-factors, e.g. drugs, malnutrition or other infections, thus, everything that weakens the immune system. This is consistent, because as soon as a co-factor is needed, the virus epidemic is at an end.

Considering the question of whether HIV is the cause of AIDS, one thing must be kept in mind, despite the dogma: the proof of a virus is not enough. There are enough harmless viruses that are not pathogenic. Added to this is the fact that the human immune system neutralizes viruses.

Here are the reasons why HIV is not the cause of AIDS.

1) In defense of the HI virus hypothesis of AIDS, it is often stated flatly that this is documented in a plethora of publications. I could not say that. While it is true that the majority of publications seek to emphasize their importance by reference to just this. But I have not seen a publication that proves that.

Yes, there is a lot of HIV research going on, billions of dollars' worth of research programs. But the statement that HIV is the cause of AIDS is regularly at the beginning of each work, usually in the very first sentence. For the proof it should be stated in the last sentence with the corresponding proofs before it. I did not notice such a publication.
In fact, if the patient was diagnosed with HIV+ and died, then he died from AIDS, i.e. from one of the 30 WHO catalog diseases, including prolonged fever, diarrhea and / or weight loss. That's the only evidence I have seen. And this in a population that is well known for heavy drug use and sexually transmitted diseases and/or treated with HAART, or that suffers from many real infections and illnesses in Africa.

It should be a small thing to name this publication; maybe it's two or three. But: the most important paper in the lives of these scientists and the basis of all their own research. And nobody knows this publication?

2) As stated above, most of the experiments are performed in vitro, i.e. in the test tube and in the absence of human antibodies. Also, these experiments are carried out with specially ***activated cells***, see above.

It is completely unclear what the equivalent of this activation is in vivo, that is in the human body. It is also very strange that viral structures can be generated by suitable stimulation in uninfected cells. This raises the question of how to discriminate against such structures under the given experimental conditions?

3) In addition, inferences from *in vitro* experiments are always problematic because they are performed in the absence of human antibodies.

It is one of the oddities of the HI virus hypothesis that although HIV antibodies serve as a bio-marker to define the disease, they are otherwise useless. Add to this the strange fact that only **zero** viruses protect against the putative disease, i.e. the supposed PCR viral load must be below the detection limit, while for all other viruses the immune defense works for latent viruses, e.g. for chickenpox.

And how does the HI virus manage to comply with the technical limits of machines? This detection limit is completely arbitrary.

4) The zoonosis theory is very constructed. It raises more questions than it answers. Why should a zoonosis in Africa around 1930 lead to an epidemic in the US in the 1980s? How likely is it that two pathogenic virus groups have emerged around 1930 in 13 or more zoonoses at the same time, which are supposed to have the same effect but differ by >45% in the gene sequences?

5) How can the contradictions in the age determination of SI and HI virus groups on the basis of *'molecular clocks*' be explained? There is no reason why they should be different in SIV and HIV. The mutation rate is the same in both cases. Analogous application of the same method for SIV and HIV results in a comparable age. At the same time, both the wide spread and the lack of pathogenicity of SIV speak for an age of several million years.

6) Why should such a viral epidemic first show up in a group of drug addicted homosexuals in San Francisco, people with frequently changing sexual partners and unprotected anal intercourse and numerous classical infections?

How likely is that?

Of all things, the supposed virus shows up for the first time in men weakened by other diseases? HI risk groups comprise mainly men (MSM - Men having sex with men). In this group also syphilis, gonorrhea, herpes and HBV are prevalent with a coincidence of >50% for syphilis and >90% for HBV. Add to that the drug addiction.

7) All statements that HIV progresses to AIDS after years come from the risk groups of the 1980s.

Only later this has been transferred to non-risk groups and these people were treated with HAART. The absence of AIDS there was then seen as evidence of the efficiency of HAART.

8) Why should an epidemic of a sexually transmitted disease, even if the heterosexual transmission rate is very low, be so strongly gendered and asymmetrical? Where is the epidemic in female, non-drug-addicted prostitutes?

9) With the multiple infections in risk groups arise the diagnostic problems, especially the CD4 cell count and the putative PCR viral load. Both are proven to be affected not only by the putative HI virus, but also by other diseases and drugs.

The presumably decreasing CD4 cell count is considered a sign of immunodeficiency, ignoring completely that the considered populations have been multiply infected, strongly drug dependent or malnourished. Regardless of any new virus, the CD4 cell count is then decreased.

As several publications show, a decrease in CD4 cell count does not always correlate with an increase in PCR viral load, see above. As evidence for a virus hypothesis, the biomarker CD4 cell count is inappropriate. And in the case of PCR viral load, co-infections and parasites and maybe also HERV are also measured.

This is not a proof for a virus or the effects of a virus.

10) Equally unfounded is the often cited argument that the alleged efficiency of HAART is exactly the proof of a virus hypothesis.

It is argued that HAART has shown that under HAART the CD4 cell count recovers and the PCR viral load decreases, to below the technical detection limit of the devices.

Here it takes its toll that one defined the illness by bio markers without any standard for healthy people or the influence of classical infections or drug use. By doing so, all control is lost over what else affects the bio-marker. This is simply ignored.

As shown above CD4 cell count can be low transiently or permanently in healthy HIV-negative people. In tuberculosis patients that are HIV-negative, it is low because of the tuberculosis, in drug addicts it is low because of the drugs. In addition, the CD4 cell count is decreased by numerous other infections, including also by sunburn.

No one has ever measured the beautiful curves of CD4 cell count and putative PCR viral load shown in the textbooks in one particular patient. Therefore, schematic curves are shown until today. In practice, these curves are chaotic for the individual patient, which is not surprising since many factors influence these values and not just HAART.

The HAART argument is also contradicted by the fact that under HAART the measured PCR viral load in between can also be increased, so-called blips, cf.

- Percus, „*The distribution of viral blips observed in HIV-1 infected patients treated with combination antiretroviral therapy*.", Bull Math Biol. **2003** Mar;65(2):263-77, https://www.ncbi.nlm.nih.gov/pubmed/12675332

That too has been known for a long time.

How should these temporary increases be caused? Resistance to HAART? Why then only temporarily, should a resistance not be permanent? Problems with the device? These blips are too common. Classical infections, e.g. flu? Difficult, because then PCR would not be HIV specific and one measures, as shown above all sorts of other things.

PCR viral load blips speak clearly against it. That HAART is still effective, is pure guesswork. But as so often in the HIV environment, the burden of proof is reversed and one has to prove the lack of effect.

There is also a point that is often neglected: PCR cannot distinguish between active and inactive viruses or viruses and virus fragments.

11) How likely is it that substances developed in the sixties in a completely different context, such as nucleoside analogues, not only have an antiviral effect but also act specifically on reverse transcriptase (RT), i.e. the virus protein that translates the viral RNA into DNA?

It is more plausible that one has seen an opportunity to reuse unsuitable substances for chemotherapy, because they are too poisonous. Without the imputed RT specific effect, however, the "*HAART acts antiviral = HIV is the cause of AIDS*" also breaks down.

This is also reflected in the wrong standards that have been created: by assuming a viral cause of AIDS from the beginning, and having set an "*increased survival rate*" as the measure of "*drug effectivity*". Increased in relation to what? That people who are strongly drug addicted and suffer from classical infections have a lower probability of survival than healthy people is obvious. That was the situation in the 80s and 90s.

12) It is noticeable that the "*patients*" live the longer the lower the drug doses are. This clearly speaks against HAART and refutes the viral theses with the same argument.

As mentioned in *Trickey et al*. there was a reduction in the ART regimes over the last 2 decades for ***Zidovudine*** (AZT) from ***59%*** to ***8%***, ***Didanosine*** from ***17%*** to ***1%***, ***Lamivudine*** from ***80%*** to ***19%*** and ***Stavudine*** from ***40%*** to ***0%***. These are strong confounding factors in life expectancy studies which cannot be ignored. We are not aware of one single study that discriminates against these factors.

At the same time the alleged efficacy of ART is one of the main arguments for the hypothesis of a viral and thus transmittable cause of the AID Syndrome.

On the ART regime changes over the years cf. to Table 2 in,

- Trickey et al., "*Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies*.", Lancet HIV. **2017** Aug;4(8):e349-e356, https://www.ncbi.nlm.nih.gov/pubmed/28501495

Zidovudine (AZT) and Lamivudine are on the *WHO Model List of Essential Medicines*. Why reduce their application?

- WHO Model List of Essential Medicines, 21st List (2019), https://www.who.int/medicines/publications/essentialmedicines/en/

"6.4.2.1 Nucleoside/Nucleotide reverse transcriptase inhibitors" [NRTI]

Abacavir (ABC), Lamivudine (3TC), Tenofovir disoproxil fumarate (TDF), Zidovudine (ZDV or AZT)

13) In the HAART patients who have been misdiagnosed as well as in case of PrEP/PEP the side effects of the drugs are clearly shown. These side effects match 1:1 the symptoms of the putative *HIV-related diseases* in contrast to *opportunistic infections* which are supposed to occur after years. Again, this shows that the alleged efficacy of HAART is no evidence for the virus hypothesis. At the same time, this refutes the very convenient theory of *Immune Reconstitution Inflammatory Syndrome* (IRIS). There is no evidence at all for this hypothesis.

14) Very striking is also the supposed extremely high mutation rate of the (very small) HI virus with its around 8000 base pairs and 9 genes, cf.

- Cuevas et al., "*Extremely High Mutation Rate of HIV-1 In Vivo*", Published online **2015** Sep 16, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4574155/

"*Our work highlights the fine balance for HIV-1 between enough mutation to evade host responses and too much mutation that can inactivate the virus*."

"*Host response*" for the supposed HI virus exists and is called "*anti-bodies*". A mutation is a purely random process. That this "*mechanism*" in each case, i.e. in every HIV+ measured human being should allow the HI virus to "*escape the immune system*", but at the same time always results in an active, reproducing virus and also unfolds its alleged harmful effects (pathogenic), is absurd.

But it is a very good argument, actually the best, for forever lasting drug research.

15) The extremely high mutation rate of HIV, cf. Cuevas et al., 2015, which should often lead to inactive pathogens, along with years of latency until it actually should come to AIDS, makes the diagnoses made on the basis of PCR (NAT) appear in a very strange light.

In non-risk groups, there is no evidence that there is anything infectious in the body of the suspected patient at all.

The pathogenicity of the suspected HI virus is also questionable since not two HIV viruses should be the same. Even in the body of HIV+ measured persons, there should be several types of viruses, as Nobel Prize winner Françoise Barré-Sinoussi (Nobel Prize 2008 together with Luc Montagnier for the discovery of the putative HI virus) points out, cf.

- Barré-Sinoussi et al., "*Expert consensus statement on the science of HIV in the context of criminal law.*", J Int AIDS Soc. **2018** Jul;21(7):e25161, https://www.ncbi.nlm.nih.gov/pubmed/30044059

"Mutations of the virus occur repeatedly so that every person living with HIV has more than one virus variant [154]. During transmission, a limited number of virus variants (one to a few) are transmitted, but these will also mutate to form new variants ***so that no two persons' HIV is identical*** *[155]."*

What is the common disease? And all these types of viruses are active, have the same characteristics and cause the same symptoms?

And all react to the same antibody tests?

16) The ***Henle-Koch postulates*** are not met by the HIV virus hypothesis of AIDS. These postulates state that 3 requirements must be met in order to prove that a certain pathogen is the cause of a particular disease:

i) The pathogen must be detectable in all cases of the disease and the pathogen may not be present in healthy people.

Here, too, the first question to ask is: what is the disease? This is defined by biomarkers, i.e. a decrease in the number of CD4 cells to the point of failure of the immune system. However, there are also many other agents in risk groups.

The fact that the HI virus is detectable in all cases has, above all, a systematic cause, namely that antibodies to a HI virus serve to define the putative disease. The correlation today is 100% - by definition. However, until the 1990s it was permissible to diagnose AIDS without HIV.

In non-risk groups we also find the Long-Term-Non-Progressors (LTNP), i.e. HIV+ people who do not progress to AIDS. Who has ever heard of Long-Term-Non-Progressors for flu, measles or chickenpox?

Applying reasonable standards, LTNP's share amounts to 20% and higher.

I would add here: the disease must not occur in healthy people. This is exactly what happens when an HIV-negative person suffers from one of the WHO's catalog diseases.

ii) The pathogen must have been isolated and bred in pure culture.

This is a controversial topic. There is little public knowledge that numerous cellular proteins can be detected, **in** but also **on** the putative HIV virus. See.

- Cantin et al., "*Plunder and stowaways: incorporation of cellular proteins by enveloped viruses*.", J Virol. **2005** Jun;79(11):6577-87, https://www.ncbi.nlm.nih.gov/pubmed/15890896

This makes detection considerably more difficult. And *detected* was reverse transcriptase activity in activated cells.

It is clear that by the time the supposed HI virus was discovered, no technical means were available to isolate the virus. And it is very doubtful that it has been achieved later.

Also, in electron micrographs viruses are very difficult to distinguish from extracellular vesicles. Cf.

- Nolte-t'Hoen et al., "*Extracellular vesicles and viruses: Are they close relatives?*", Proc Natl Acad Sci USA. **2016** Aug 16; 113(33): 9155–9161, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4995926/

"Physical and chemical characteristics of many EVs, as well as their biogenesis pathways, resemble those of retroviruses. Moreover, EVs generated by virus-infected cells can incorporate viral proteins and fragments of viral RNA, ***being thus indistinguishable from defective (noninfectious) retroviruses****"*

Also, in this context, the oddity is that it is possible to industrially grow infected T cells to produce HIV Ag / Ab tests, but on the other hand, the HI virus is said to kill those very cells. That too does not fit together.

iii) The pathogen must cause the disease in a healthy animal (animal experiment).

Apes do not get AIDS, see above.

17) There are increasingly marketing efforts, especially on Youtube to make of HIV a kind of flu to force the early onset of HAART. Nevertheless, there are these very long and strongly fluctuating latencies of several years to decades from a supposed HIV infection to the presumed occurrence of immunodeficiency. If there are classical infections, e.g. in risk groups, the CD4 cell count is not a reliable bio marker.

And it should not be forgotten that the diseases in the WHO AIDS catalog have been around for a long time, independently of HIV+ or HIV-. Taking the adverse effects of HAART into account it is doubtful that HAART is the cause of anything positive.

The long latencies clearly speak against a viral cause. In viral infections, infection and disease are in a direct temporal relationship, which is due to the cell division rate of the host cells and the proliferation of viruses. Therefore, infections cause symptoms after a few days.

What should happen in these years? Between an HIV infection and the onset of the supposed disease are numerous other minor and severe infections with real pathogens.

The entire concept of *slow virus* is very questionable and seems artificial. In addition to HIV, this also applies to other viruses, e.g. HPV, which after years (better decades) shall cause cancer.

18) The bystander cell problem, which has been kept from the public discussion for years, shows that one does not know the mechanism of action of HIV / AIDS. An HIV+ measured person regenerates CD4 cells in large numbers every day and is not immunosuppressed. The detection of anything retroviral, particularly in specially activated cell, is no proof of causality.

19) In addition, there is the HERV problem as well as the numerous cross-reactions that make the assignment of reverse transcriptase activity to the HI virus difficult. Very remarkable are also the serological cross reactions of HERV epitopes and HIV antibodies on the one hand and the omnipresent relationship between HERV and various other diseases (including cancer) on the other hand. What if an HIV signal is simply a sign of stressed cells? The theory was completely developed on people with multiple diseases.

In far too many publications, one has relied on supposed HIV detection and ignored other possible factors, for example, in Africa chronic malnutrition, classical epidemics or parasites. So you can always generate causality. Just ignore all other parameters.

20) Statistics from Africa are very problematic because usually there is no reporting system. Partly in the statistics, people who do not report back (*lost to follow-up*) are counted as dead. Cf.

- Wandeler et al., "*Trends in life expectancy of HIV-positive adults on antiretroviral therapy across the globe: comparisons with general population.",* Curr Opin HIV AIDS. **2016** Sep;11(5):492-500, https://www.ncbi.nlm.nih.gov/pubmed/27254748

"The study from Uganda, and the analysis of the Canadian Observational Cohort collaboration assumed that 30% of patients lost to follow-up had died whereas in Rwanda, investigators assumed that about 50% of patients lost to follow-up had died."

One can get the impression that it depends on what the statistics should show. Either one wants to point out the urgency of the problem (*many supposed AIDS deaths*) or one would like to prove the alleged efficiency of HAART (*few supposed AIDS dead*).

And what does "*died of AIDS*" mean? Which of the approximately 30 catalog diseases? Here, any breakdown is usually missing, whether it was e.g. tuberculosis and / or whether the human has suffered from other diseases or parasites.

21) At the same time, increases in case numbers in the statistics are mainly due to adaptations of the counting method, most recently with a further splitting of the diagnosis in HIV stages, which depends exclusively on the very dubious CD4 cell count. I do not see how these statistics should discriminate against classical infections that have been shown to decrease the CD4 cell count.

22) Also, the subsequent introduction of *HIV-related diseases*, which supposedly are caused directly by the putative HIV virus, i.e. without favoring opportunistic infections by immunosuppressive effects, seems to me strongly constructed. This was only discovered when they started to roll out HAART on a large scale. At the same time, the **match with side effects of HAART is 100%.** This is not least shown by the severe damage up to death caused in misdiagnosed HIV-negative people on HAART.

For such a small virus, that would be a lot of very different diseases. A virus, which, as we have seen above, also mutates very strongly and at the same time by destruction of CD4 cells, in spite of the bystander cell problem, should lead to immunosuppression.

23) The statistical data lack an exponential increase, as would be typical of a transmissible disease caused by a new pathogen.

24) While in the past false positives by cross-reactions have been played down and manufacturers boasted with specificities and sensitivities close to 100%, today one remembers the prevalence (frequency) as a factor for the PPV (positive predictive value) and surmises that the high numbers of false positive test results are attributable to the decreasing prevalence of HIV due to HAART and PrEP.

Regardless of the adverse effects of PrEP and HAART, there is not the slightest proof of this. It is a pure guess.

The impression is that nothing has changed in the last 30 years on the false positives, but that these make up a more or less constantly high proportion while occurring more frequently in pregnant women. This also speaks in favor of a very fundamental problem with these bio markers.

25) Immunosuppression can be explained much more directly and more plausibly by drug abuse, especially nitrites (poppers) and classical infections. These are very common in the so-called risk groups (MSM - Men having sex with men), see Appendix III.

26) No classic pathogen leads to a chronic disease in ***100%*** of cases in therapy, and this for all age groups, all races and both genders.

27) Many of the reasons given here are not new. What is new is that as far as possible current publications were used. Due to the very one-sided "*research*" in the last 30 years, this is not always possible.

However, I do not see an error in the work of Dr. Duesberg, neither methodically nor content wise. Cf.

- Duesberg, „*Human immunodeficiency virus and acquired immunodeficiency syndrome: correlation but not causation*.", Proc Natl Acad Sci USA. **1989** Feb;86(3):755-64, https://www.ncbi.nlm.nih.gov/pubmed/2644642

In order for the virus hypothesis of AIDS to be correct, Dr. Duesberg must have been wrong in every single argument. I do not believe that.

It is a particular feature of the HIV / AIDS discussion that it is conducted in the manner of a war of faith and that critics are excluded for research. This also does not inspire confidence in the virus hypothesis of AIDS.

28) Research focuses primarily on the molecular level, i.e. the single protein and the single molecule. On the one hand, this obstructs the view on the relations on a larger scale. At the same time, it has not resulted in finding the basic molecular mechanism of how HIV leads to AIDS. Only through a variety of ad hoc assumptions and selective reading of the data, e.g. ignoring all factors except HIV, this theory (*HIV = AIDS*) can be stabilized to some extent. These are clear signs of a failed theory.

29) There remains one question: how can "*research*" be so misguided?

For people with some research experience, this is not difficult to understand: Research is based on the herd principle. There are the bellwethers who say how to interpret the results, and the vast majority are happy when the research grant (= money) is approved.

The bellwethers also regularly participate in the search committees for university chairs or make recommendations on how to fill positions in commissions or ministries. This network is very dense and it creates significant dependencies. Anyone who is noticed for too critical thoughts can quickly forget about his or her research career.

HIV means big money and until very recently great fame, e.g. by a Nobel Prize or the Federal Cross of Merit (on ribbon). This works so well because all critical questions are ignored.

Research funding is scarce and biomedical research is extremely expensive. This creates additional pressure, not only to publish but also to publish "*groundbreaking*" results. Or just commercially utilizable things such as anti-body patents or new diagnostic procedures, see He et al., 2018, above.

However, after the HI virus hypothesis had been decided in the 1980s, with direct involvement of the then US government, there was probably no way back. The aggressiveness of the attacks against dissident scientists as expressed in the "*contributions*" of Mr. Kalichmann, and by which he apparently earns his money, clearly show how thin-skinned one was and is. No wonder, after more than 20 years of HAART there is only the way forward.

Taking into account known human weaknesses such as greed, arrogance, megalomania and craving for recognition, on the one hand, and sycophancy and servile flattery on the other hand, along with simple stupidity, these personal attacks also seem to speak against the HI virus hypothesis.

24. Formation of a theory

It is a permanent flaw of the HIV / AIDS hypothesis that is was promulgated by Heckler and Gallo in 1984 without any peer review and without sufficient evidence. The available data shows that the theory formation on AIDS and the cause of AIDS-defining diseases is not complete.

The available data are **not** compatible with the theory that AIDS is caused by a virus that is transmitted primarily sexually or through blood. This is the prevailing opinion and by far the most lucrative interpretation. But there are too many doubts that this interpretation is false. Far too many doubts to justify a HAART therapy.

The available data are compatible with the following theories on AIDS (**because this is all about AIDS**):

a) **HIV is a harmless passenger virus transmitted predominantly sexually or through blood**. The real cause of AIDS is drugs, treatment or malnutrition, cf.

Duesberg et al. „*The chemical bases of the various AIDS epidemics: recreational drugs, anti-viral chemotherapy and malnutrition.*“, J Biosci. **2003** Jun;28(4):383-412 https://www.ncbi.nlm.nih.gov/pubmed/12799487

Duesberg, „*Human immunodeficiency virus and acquired immunodeficiency syndrome: Correlation but not causation*”, Proc. Nati. Acad. Sci. USA Vol. 86, pp. 755-764, Feb **1989**, http://www.pnas.org/content/pnas/86/3/755.full.pdf

Duesberg et al. *„AIDS since 1984: No evidence for a new, viral epidemic – not even in Africa*”, IJAE, Vol . 116, n. 2: 73-92, **2011**, https://www.ncbi.nlm.nih.gov/pubmed/22303636

Haverkos et al., „*Nitrite Inhalants: History, Epidemiology, and Possible Links to AIDS*”, Env. Health. Persp. Vol 102 (10), Oct. **1994**, https://www.ncbi.nlm.nih.gov/pubmed/9644194

Dax et al., „*Effects of Nitrites on the Immune System of Humans*“, in NIDA Research Monograph 83, Health Hazards of Nitrite Inhalants, Ed. Haverkos und Dougherty, **1988**, p. 75, https://archives.drugabuse.gov/sites/default/files/monograph83.pdf

b) **The detected antibodies do not belong to a specific virus reaction. The detection of a viral antigen is pending.** This would again bring drugs to the forefront as an AIDS cause, cf.

Papadopulos-Eleopulos et al. „*A critique of the Montagnier evidence for the HIV/AIDS hypothesis.*“, Med Hypotheses. **2004**; 63(4):597-601, https://www.ncbi.nlm.nih.gov/pubmed/15325002

More references under: http://www.theperthgroup.com

Especially, July, **2017**, http://theperthgroup.com/HIV/TPGVirusLikeNoOther.pdf

c) **HIV is necessary but not sufficient**. It needs more co-factors. Here are drugs possible, but also malnutrition (especially in developing countries) or multiple infections (classical infections, parasites), cf.

Root-Bernstein, „*Five myths about AIDS that have misdirected research and treatment*", Genetica 95:111-132, **1995**, https://www.researchgate.net/profile/Robert_Root-Bernstein/publication/226734006

Root-Bernstein, „*The necessity of cofactors in the pathogenesis of AIDS: a mathematical model.*", J Theor Biol. **1997** Jul 7;187(1):135-46, https://www.ncbi.nlm.nih.gov/pubmed/9236115

25. Concluding remarks

We probably have to familiarize ourselves with the idea that frequent unprotected anal intercourse with changing partners and intensive drug use (Crystal, Ecstasy, Chemsex, ...) along with numerous classical infections (syphilis, HBV, herpes, gonorrhea, ..) and probably not insignificant sleep deprivation does not do good to the immune system.

That holds true with or without the putative detection of reverse transcriptase (RT) activities. But it corresponds to the originally affected population in the 70s and 80s in San Francisco. People who are being treated for HIV today, especially women and children, have nothing in common with this population, possibly not even a virus whose pathogenic effects remain open. And this especially in the presence of antibodies.

One should not summarize about 30 old known diseases under a new label and define an epidemic. It seems that science has created a self-fulfilling prophecy and this in several ways,

a) by the drugs prescribed, whose side effects are only insignificantly different from a whole range of symptoms of the suspected diseases.

b) by criteria that are almost not distinguishable in developing countries from already existing catastrophes or are favored by them (malnutrition, parasites, ...)

c) by ignoring the drug addiction problem that is constantly creating new cases.

d) and ultimately also through stigmatization and exclusion of those affected. That should not be underestimated in its effect. The suicide numbers speak for themselves.

Most people probably have no idea of the hygienic conditions in developing countries. And probably also not of the nutritional situation there. Here an "*acquired immunodeficiency*" comes in handy, that continues to distract from the real problems in Africa and elsewhere. And which politician would like to have a discussion that there is a massive drug problem in his or her country?

There are many indications that during the last 30 years the methods (antibody tests, CD4 cell count, PCR) have been developed on the living object, i.e. the patient, with necessary refinements if the results did not fit. This *designs* results fitting the theory. Or the results are declared as no longer relevant, as in the case of the CD4 cell count.

The nature of HIV and AIDS can only be understood when it is realized that it is a forced agreement on how the current data is to be interpreted. This is not a scientific basis. This agreement rests on a very dubious basis, both methodologically and in substance. But it is the most lucrative of all alternatives.

The practice of *scientific consensus opinion* is reflected again in the social consensus that leads to the exclusion of the *ill-declared*. HIV/AIDS is therefore a social problem in two ways. Once within the *consensus culture* of the so-called scientists, who single out individuals using biomarkers (and who can live quite well from this). And secondly, in society, to which not much more remains than to adopt this segregation without questioning.

That the controversy carries inquisitorial traits and treats dissidents as heretics is no coincidence. Much of the HI virus hypothesis of AIDS is based on assumptions. These one can believe or not.

But nature does not give much on the consensus of scientists. Scientific standards have been developed for this very reason.

And none of this I read on Wikipedia.

26. Further references

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Bauer, "*HIV Tests Are Not HIV Tests*", J Am Phys and Surg Vol 15 (1) Spring **2010**, http://www.jpands.org/vol15no1/bauer.pdf

Papadopulos-Eleopulos, "*Reappraisal of AIDS - is the oxidation induced by the risk factors the primary cause?*", Med Hypotheses, **1988** Mar;25(3):151-62, https://www.ncbi.nlm.nih.gov/pubmed/3285143

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House of Numbers, Anatomy of an epidemic, **2009** (http://www.houseofnumbers.com)
https://www.youtube.com/watch?v=Vq8gT0xUcKY

Positively False? (**2011**)
http://www.positivelyfalsemovie.com/

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HIV equals AIDS - Fact or Fraud?
https://www.youtube.com/watch?v=XZKl0tozbco

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https://www.youtube.com/watch?v=QS0i1LiHG5U

AIDS - Die großen Zweifel - Arte (**1996**) - überarbeitet
https://www.youtube.com/watch?v=pp8mL3r7m1I

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Rethinking AIDS
http://rethinkingaids.com/

Virusmyth
http://www.virusmyth.com/aids/index.htm

27. Annex I: Calculation of the PPV for HIV self-tests in non-risk groups

The PPV, or positive predictive value (PPV), is a statistical quantity that describes for a given test with what probability a human is really sick on a positive test result. That's the value that interests a suspected patient.

In the PPV enters the specificity and sensitivity of the test, but also the (real) frequency (prevalence) of the disease to be tested. In rare diseases, and HIV is one of them, the PPV is very small, although sensitivity and specificity are >98%. Sensitivity and specificity are visually high and that's what manufacturers report.

As HIV risk groups, science refers to gay men (MSM) who often have changing sexual partners and / or frequently use drugs. Non-risk groups are heterosexual people, not drug addicts, monogamous or protected intercourse and not drug addicted women, cf.

- Bush *et al.* „*HIV is rare among low-risk heterosexual men and significant potential savings could occur through phone results*.", Sex Health. **2010** Dec;7(4):495-7, https://www.ncbi.nlm.nih.gov/pubmed/21062593

- Liu *et al.* "*The false-positive and false-negative predictive value of HIV antibody test in the Chinese population*", Journal of Medical Screening, **2008**, Vol. 15 No. 2, https://www.ncbi.nlm.nih.gov/pubmed/18573774

The prevalence of HIV in non-risk groups can be estimated from the data of the Robert Koch Institute (RKI) for risk groups, cf. https://www.rki.de/DE/Content/Infekt/EpidBull/Archiv/2017/Ausgaben/47_17.pdf?__blob=publicationFile (S. 535)

HIV/AIDS in Deutschland – Eckdaten der Schätzung*

Epidemiologische Kurzinformation des Robert Koch-Instituts, Stand: Ende 2016

		Geschätzte Zahl der Menschen, die Ende 2016 mit HIV/AIDS in Deutschland leben		
		insgesamt	mit HIV-Diagnose	ohne HIV-Diagnose
	Gesamtzahl	> 88.400 (81.500 – 94.700)	75.700 (69.400 – 81.900)	> 12.700 (12.100 – 13.400)
	Männer	> 71.900 (66.400 – 76.700)	61.200 (56.000 – 66.000)	> 10.700 (10.100 – 11.300)
	Frauen	> 16.600 (14.900 – 18.000)	14.600 (13.100 – 15.900)	> 2.000 (1.800 – 2.300)
Inland [1] (nach Infektionsweg)	Sex zwischen Männern	56.100 (52.000 – 59.900)	46.900 (43.200 – 50.500)	9.200 (8.700 – 9.700)
	Heterosexuelle Kontakte	11.200 (10.000 – 12.200)	8.500 (7.400 – 9.400)	2.700 (2.400 – 3.000)
	i.v. Drogengebrauch	8.200 (7.300 – 9.100)	7.400 (6.500 – 8.200)	800 (640 – 990)
	Blutprodukte [3]	– 450	– 450	keine
Ausland [2] (nach Herkunfts-region)	Europa	> 3.000 (2.700 – 3.400)	3.000 (2.700 – 3.400)	nicht bestimmbar
	Asien	> 1.400 (1.200 – 1.600)	1.400 (1.200 – 1.600)	nicht bestimmbar
	Afrika	> 6.400 (5.600 – 7.200)	6.400 (5.600 – 7.200)	nicht bestimmbar
	Amerika/Ozeanien	> 770 (680 – 880)	770 (680 – 880)	nicht bestimmbar
Davon unter antiretroviraler Therapie			64.900 (62.600 – 67.200)	

The prevalence in risk groups for Germany is about 1 in 1000. The prevalence in non-risk groups can be derived from literature data:

Autoren	Jahr	Titel	HIV-positiv	Grundgesamtheit	Anteil	Link
Kleinmann *et al.*	1998	*False-Positive HIV-1 Test Results in a Low-Risk Screening Setting of Voluntary Blood Donation*	421	5.020.000	0,0000838645	[1]
Burke *et al.*	1988	*Measurement of the False Positive Rate in a Screening Program for Human Immunodeficiency Virus Infections*	14	135.187	0,0001035603	[2]
MacDonald *et al.*	1989	*Performance Characteristics of Serologic Tests for Human Immunodeficiency Virus Type 1 (HIV-1) Antibody among Minnesota Blood Donors: Public Health and Clinical Implications*	17	290.110	0,0000585985	[3]
Busch *et al.*	1991	*Evaluation of Screened Blood Donations for Human Immunodeficiency Virus Type 1 Infection by Culture and DNA Amplification of Pooled Cells*	1	61.171	0,0000163476	[4]
Bush *et al.*	2010	*HIV is rare among low-risk heterosexual men and significant potential savings could occur through phone results.*	6	17958	0,0003341129	[5]
Liu *et al.*	2008	*The false-positive and false-negative predictive value of HIV antibody test in the Chinese population.*	11	1.195.286	0,0000092028	[6]
				Mittelwert	**0,0001009478**	**=(1:10.000)**

With data from:

[1] https://jamanetwork.com/journals/jama/fullarticle/188011
[2] https://www.nejm.org/doi/full/10.1056/NEJM198810133191501
[3] http://annals.org/aim/article-abstract/703044/performance-characteristics-serologic-tests-human-immunodeficiency-virus-type-1-hiv
[4] https://www.nejm.org/doi/full/10.1056/NEJM199107043250101
[5] https://www.ncbi.nlm.nih.gov/pubmed/21062593
[6] https://www.ncbi.nlm.nih.gov/pubmed/18573774

This results in an (estimated) prevalence for non-risk groups of about 1 in 10,000, i.e. about 10% of the prevalence of risk groups.

Sensitivity and specificity are based on WHO data, here the minimum requirements for HIV Ag / Ab Test, cf.

- WHO, *"HIV assays operational characteristics: HIV rapid diagnostic tests (detection of HIV-1/2 antibodies)"*, **2013**, p. 10, table 1, http://www.who.int/diagnostics_laboratory/evaluations/hiv/131107_hiv_assays17_final.pdf

Table 1. Specific considerations for selection of HIV diagnostics

Parameter	Considerations
Performance characteristics	
Clinical sensitivity	Set the minimum acceptable criteria e.g. ≥99% for RDTs, 100% for EIAs
Clinical specificity	Set the minimum acceptable criteria e.g. ≥98% for RDTs and EIAs
Seroconversion sensitivity	Important for blood screening and suspected highly incident populations
Inter-reader variability, if subjectively read format	Set the minimum acceptable criteria e.g. ≤5%
Invalid rate (devices/test results)	Set the minimum acceptable criteria e.g. ≤5% or ≤1%, depending on the assay format

That Sensitivity and specificity are 99% and 98% respectively. However, these values may already be too high, cf.

- Kosack et al., "*Towards more accurate HIV testing in sub-Saharan Africa: a multi-site evaluation of HIV RDTs and risk factors for false positives.*", J Int AIDS Soc. **2017** Mar 24;19(1):21345, https://www.ncbi.nlm.nih.gov/pubmed/28364560

"., individual RDTs performed more poorly than in the WHO evaluations: only one test met the recommended thresholds for RDTs of ≥99% sensitivity and ≥98% specificity."

However, assuming these values, the PPV can be calculated as follows:

Daten Input			**Vierfeldertafel**			
			Testergebnisse	Echte Diagnose		Summe
				Kranke	***Gesunde***	
Sensitivität --> Kranke (=pos) richtig erkennen	0,99	*= Se*				
Spezifität --> Gesunde (=neg) richtig erkennen	0,98	*= Sp*				
HIV Infizierte in D (vorwiegend Risikogruppen)	88.400	*= Inf*	***Test positiv***	**107**	**19.998**	*20.105*
				*A = Se * K (A = Echte Kranke)*	*B = (1 -Sp) * G (B = Falsche Kranke)*	*= A + B*
Gesamtbevölkerung	82.000.000	*= GesB*				
= Anteil der Gesamtbevölkerung	0,001078049	*= Inf/GesB*	***Test negativ***	**1**	**979.894**	*979.895*
				*C = (1-Se) * K (C= Falsche Gesunde)*	*D = Sp * G (D= Echte Gesunde)*	*= C + D*
Verhältnis Nicht- zu Hoch-Risikogruppe	0,1	*= r*				
=Häufigkeit (=Prevalence)	0,000107805	*prev = r * Inf/GesB*	Summe	*108*	*999.892*	*1.000.000*
in Nicht-Risikogruppen				*Kranke K = prev * tg*	*Gesunde G = (1 - prev) * tg*	*= tg*
Testgruppe	1.000.000	*= tg*				

Positiver Vorhersagewert des Tests: PPV (%) **0,530858533** *A/(A+B) (= % richtig erkannte Kranke unter positiv Getesteten)*

Negativer Vorhersagewert des Tests: NPV (%) 99,99988998 *D/(C+D) (= % richtig erkannte Gesunde unter den negativ Getesteten)*

The PPV (Positive Predictive Value) in non-risk groups is 0.0053 or **0.53%.** That's the ratio of "*real sick*" to "*all positive-tested*". In other words: **1 real patient in about 200 positive-tested**.

That's not very much. These tests should not be taken lightly.

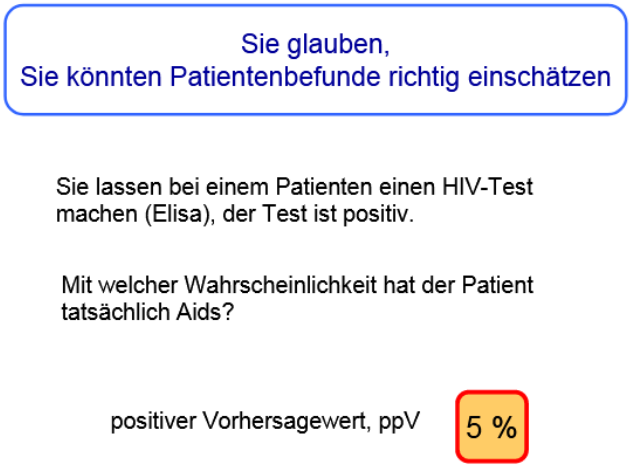
Comments on the PPV:

- Sensitivity "*affects*" the (few) ill persons. Therefore, the risk of overlooking a patient is low in absolute terms.
- Specificity "*affects*" the (many) healthy people. Here, the deviation of 100% is dominant and results in rare diseases in many "*false-positives*".
- The *positive predictive value* which is of interest for the tested is low for rare diseases.

Another example**: 58. Ärztekongress Berlin/Charité**, H.-J. Koubenec, Täuschung und Manipulation mit Zahlen, 4.11.**2010**, (Folie 3),

Translation:

58. Congress for Physicians Berlin/Charité, H.-J. Koubenec, Deception and manipulation with numbers, 4.11.**2010**, (slide 3)



Aus H.-J. Koubenec, Täuschung und Manipulation mit Zahlen, 4.11.2010, slide 3, http://www.brustkrebs-info.de/patienten-info/mammographie-screening/Le_Teil1_Taeuschung_ZahlenAEKB2010.pdf

or http://docplayer.org/39350731-Taeuschung-und-manipulation-mit-zahlen.html

Cf. also

- Walter Krämer, „*Unstatistik des Monats: ‚Sie sind wahrscheinlich HIV-Positiv'*“, 08.01.**2019**, https://www.achgut.com/artikel/unstatistik_des_monats_sie_sind_wahrscheinlich_hiv_positiv

„‚Sie sind wahrscheinlich HIV-positiv' bedeutet also, dass die Wahrscheinlichkeit bei nur etwa 8 Prozent liegt, dass man infiziert ist. [wenn Test positiv]“

*„Bei Heterosexuellen ohne Risikoverhalten, dem größten Teil der Deutschen, ist die Wahrscheinlichkeit infiziert zu sein [wenn Test positiv] nochmals deutlich kleiner, **sie liegt unter 5 Prozent**.“*

Translation

„'You are probably HIV positive' means that the probability is only about 8 percent that you are infected. [if test positive]“

"For heterosexuals without risk-taking behavior, the majority of Germans, the probability of being infected [if test positive] is even smaller, is less than 5 percent."

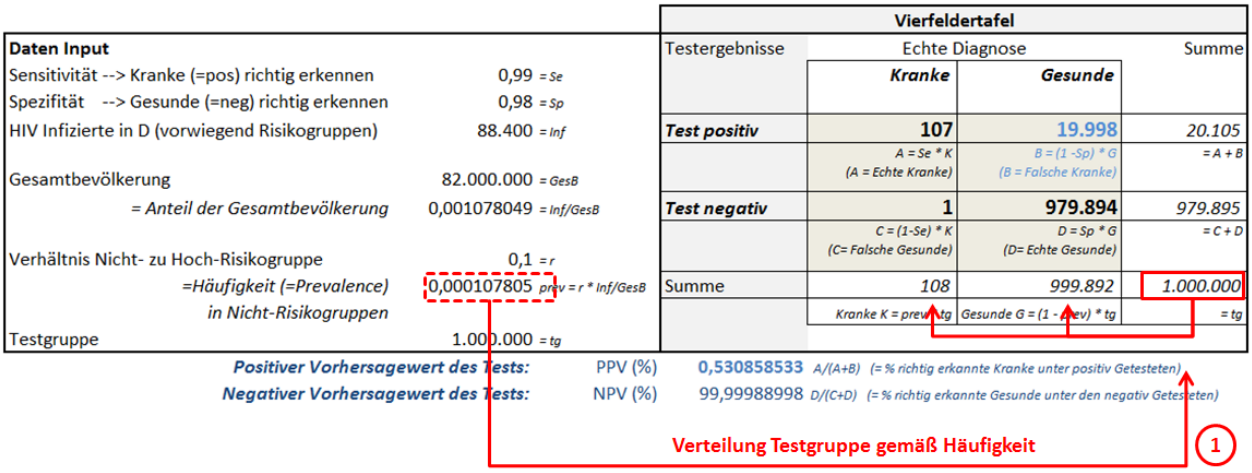
One should not rely too much on the possibility if physicians know this situation, cf.

- Manrai et al., “*Medicine's uncomfortable relationship with math: calculating positive predictive value*.”, JAMA Intern Med. **2014** Jun;174(6):991-3, https://www.ncbi.nlm.nih.gov/pubmed/24756486

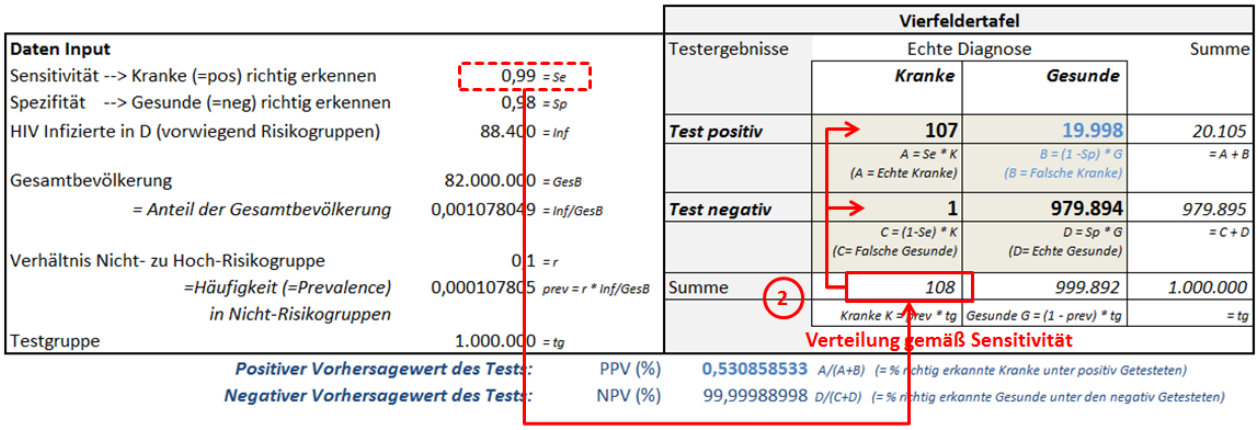
*“Approximately **three-quarters of respondents answered the question incorrectly**, …”*

27.1. Calculation steps for the PPV of HIV self-tests

Step 1:
Distribute the test group according to frequency (= prevalence)
The frequency results from => sick / total population * factor-non-risk group.



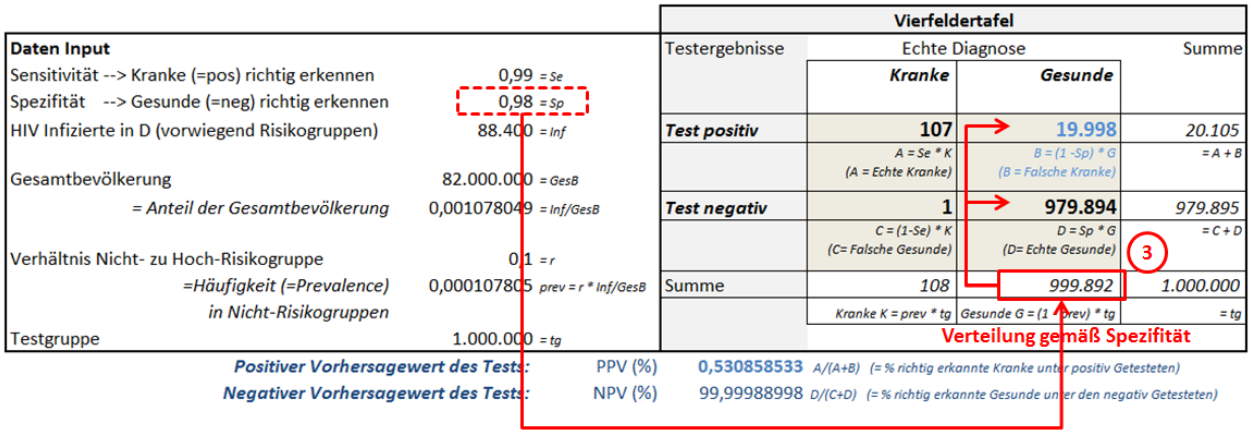
Step 2:
Distribution of patients according to sensitivity (= proportion of correctly diagnosed patients)
→ Real sick (sick + positive test)



Step 3:

Distribution of healthy people according to specificity (= proportion of correctly recognized healthy persons)

→ Real healthy (healthy + negative test)



Daten Input			Vierfeldertafel			
			Testergebnisse	Echte Diagnose		Summe
				Kranke	**Gesunde**	
Sensitivität --> Kranke (=pos) richtig erkennen	0,99	= Se				
Spezifität --> Gesunde (=neg) richtig erkennen	0,98	= Sp				
HIV Infizierte in D (vorwiegend Risikogruppen)	88.400	= Inf	**Test positiv**	**107**	19.998	*20.105*
				*A = Se * K (A = Echte Kranke)*	*B = (1 -Sp) * G (B = Falsche Kranke)*	*= A + B*
Gesamtbevölkerung	82.000.000	= GesB				
= Anteil der Gesamtbevölkerung	0,001078049	= Inf/GesB	**Test negativ**	**1**	**979.894**	*979.895*
				*C = (1-Se) * K (C= Falsche Gesunde)*	*D = Sp * G (D= Echte Gesunde)*	*= C + D*
Verhältnis Nicht- zu Hoch-Risikogruppe	0,1	= r				
=Häufigkeit (=Prevalence) in Nicht-Risikogruppen	0,000107805	prev = r * Inf/GesB	Summe	*108*	*999.892*	*1.000.000*
				*Kranke K = prev * tg*	*Gesunde G = (1 - prev) * tg*	*= tg*
Testgruppe	1.000.000	= tg				

3

Verteilung gemäß Spezifität

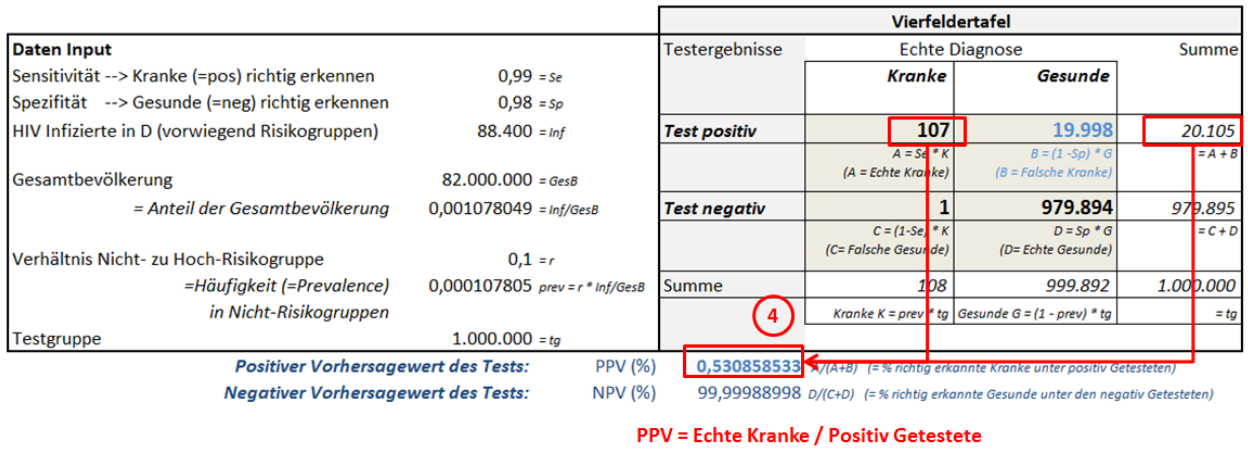
Positiver Vorhersagewert des Tests: PPV (%) 0,530858533 *A/(A+B) (= % richtig erkannte Kranke unter positiv Getesteten)*

Negativer Vorhersagewert des Tests: NPV (%) 99,99988998 *D/(C+D) (= % richtig erkannte Gesunde unter den negativ Getesteten)*

Step 4:

Calculation PPV (Positive Predictive Value)

→ Real sick (sick + positive test) to all positive-tested



Daten Input			Vierfeldertafel			
			Testergebnisse	Echte Diagnose		Summe
				Kranke	**Gesunde**	
Sensitivität --> Kranke (=pos) richtig erkennen	0,99	= Se				
Spezifität --> Gesunde (=neg) richtig erkennen	0,98	= Sp				
HIV Infizierte in D (vorwiegend Risikogruppen)	88.400	= Inf	**Test positiv**	**107**	19.998	*20.105*
				*A = Se * K (A = Echte Kranke)*	*B = (1 -Sp) * G (B = Falsche Kranke)*	*= A + B*
Gesamtbevölkerung	82.000.000	= GesB				
= Anteil der Gesamtbevölkerung	0,001078049	= Inf/GesB	**Test negativ**	**1**	**979.894**	*979.895*
				*C = (1-Se) * K (C= Falsche Gesunde)*	*D = Sp * G (D= Echte Gesunde)*	*= C + D*
Verhältnis Nicht- zu Hoch-Risikogruppe	0,1	= r				
=Häufigkeit (=Prevalence) in Nicht-Risikogruppen	0,000107805	prev = r * Inf/GesB	Summe	*108*	*999.892*	*1.000.000*
			4	*Kranke K = prev * tg*	*Gesunde G = (1 - prev) * tg*	*= tg*
Testgruppe	1.000.000	= tg				

Positiver Vorhersagewert des Tests: PPV (%) 0,530858533 *A/(A+B) (= % richtig erkannte Kranke unter positiv Getesteten)*

Negativer Vorhersagewert des Tests: NPV (%) 99,99988998 *D/(C+D) (= % richtig erkannte Gesunde unter den negativ Getesteten)*

PPV = Echte Kranke / Positiv Getestete

27.2. HIV self-tests in women

According to the data of the RKI it is found that women are measured about 4 - 5x less frequently HIV+.

Daten Input			**Vierfeldertafel**			
			Testergebnisse	Echte Diagnose		Summe
				Kranke	***Gesunde***	
Sensitivität --> Kranke (=pos) richtig erkennen	0,99	= Se				
Spezifität --> Gesunde (=neg) richtig erkennen	0,98	= Sp				
HIV Infizierte in D (vorwiegend Risikogruppen)	88.400	= Inf	***Test positiv***	**25**	19.999	*20.024*
				*A = Se * K (A = Echte Kranke)*	*B = (1 -Sp) * G (B = Falsche Kranke)*	*= A + B*
Gesamtbevölkerung	82.000.000	= GesB				
= Anteil der Gesamtbevölkerung	0,001078049	= Inf/GesB	***Test negativ***	**0**	**979.975**	*979.976*
				*C = (1-Se) * K (C= Falsche Gesunde)*	*D = Sp * G (D= Echte Gesunde)*	*= C + D*
Verhältnis Nicht- zu Hoch-Risikogruppe	0,1	= r				
Verhältnis Frauen / Männer	0,23	= f				
=Häufigkeit (=Prevalence)	0,000025071	prev = f * r * Inf/GesB	Summe	*25*	*999.975*	*1.000.000*
in Nicht-Risikogruppen ***nur Frauen***				*Kranke K = prev * tg*	*Gesunde G = (1 - prev) * tg*	*= tg*
Testgruppe	1.000.000	= tg				

Positiver Vorhersagewert des Tests: PPV (%) **0,123950248** *A/(A+B) (= % richtig erkannte Kranke unter positiv Getesteten)*

Negativer Vorhersagewert des Tests: NPV (%) 99,99997442 *D/(C+D) (= % richtig erkannte Gesunde unter den negativ Getesteten)*

According to the data of the RKI, 1 real patient results in about 800 positive-tested (= 0.124%). With this very low prevalence in women in non-risk groups, one can also ask what is actually being measured there, also given the cross-reactions in the tests.

27.3. Evaluation of the results

To evaluate this result for non-risk groups, it is often argued that the sensitivity and specificity of HIV self-tests are close to 100% and therefore there is no problem.

This is not correct, because that does not apply to rare diseases. In addition, the "*problem of women*" (see above) is ignored. And you rely too much on the manufacturer's information. The phenomenon of cross-reactions of the tests shows that 100% cannot exist. Also, the complicated WHO method (with the suppression of the result "*indeterminate*") makes the value of 99% or 98% (= minimal acceptance criterion of the WHO) for sensitivity and specificity seem plausible, see link above.

It is then often stated that it is a sum of tests, i.e. 3 tests with 98% specificity each would again come close to 100%.

This is not correct, because, what is the individual HIV self-test needed for? In addition, only the PPV is of interest to the patient and it is very low, especially in rare diseases. Here, you can test a long time.

And who says that further tests are independent and do not test the same again? This would explain the indeterminate test series found in non-risk groups.

Here is an example from 2015 - 2017, in which it took 18 months until the false positive was confirmed, cf.,

- Lang *et al*., "*HIV misdiagnosis: A root cause analysis leading to improvements in HIV diagnosis and patient care*", J. Clin. Viro. 96 (**2017**), 84 - 88, https://www.ncbi.nlm.nih.gov/pubmed/29031156

In non-risk groups, the result "*indeterminate*" occurs more frequently, i.e. the reactions (bands) give no clear result. These people often go through different results in subsequent tests: positive, indeterminate, negative, positive, negative, indeterminate…

→ A bad test does not get better if you repeat it.

Cf. also

- Shanks et al. "*Evaluation of HIV testing algorithms in Ethiopia: the role of the tie-breaker algorithm and weakly reacting test lines in contributing to a high rate of false positive HIV diagnoses."*, BMC Infect Dis. **2015** Feb 3;15:39, https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-015-0769-3

"*The risk of false positive HIV diagnosis in a tiebreaker algorithm is significant*."

Note: a Tie-Breaker test consists of 2 or 3 tests, with the 3rd test deciding at 1: 1 of the first two tests, cf. Shanks: "*In Ethiopia a tiebreaker algorithm using 3 rapid diagnostic tests (RDTs) in series is used to diagnose HIV. Discordant results between the first 2 RDTs are resolved by a third 'tiebreaker' RDT.* "

28. Annex II: Further PCR problem cases or what DNA = DNA means for the methodology

The PCR problems outlined above for HIV are also found in the diagnosis of other organisms. The problems are caused by the methodology itself: **DNA is DNA**. This is the same for all organisms, whether fungus, bacteria, virus, plant, animal or human.

Here statements from the **textbook** „*Biochemistry*“, 5th Edition, Berg, Tymoczko and Stryer, https://www.ncbi.nlm.nih.gov/books/NBK22409/ (format adapted):

“Several features of this remarkable method for amplifying DNA are noteworthy.

***First, the sequence of the target need not be known**. All that is required is knowledge of the flanking sequences.*

Second, the target can be much larger than the primers. Targets larger than 10 kb have been amplified by PCR.

***Third, primers do not have to be perfectly matched to flanking sequences to amplify targets.** With the use of primers derived from a gene of known sequence, it is possible to search for variations on the theme. In this way, families of genes are being discovered by PCR.*

*Fourth, PCR is highly specific because of the stringency of hybridization at high temperature (54°C). Stringency is the required closeness of the match between primer and target, which can be controlled by temperature and salt. At high temperatures, **the only DNA that is amplified is that situated between primers that have hybridized**. A gene constituting less than a millionth of the total DNA of a higher organism is accessible by PCR.*

*Fifth, PCR is exquisitely sensitive. **A single DNA molecule can be amplified and detected“.***

One molecule is enough. But one molecule is certainly not pathogenic. And as we have read, primers just do not have to fit perfectly: “*Third, primers do not have to be perfectly matched to flanking sequences to amplify targets.*" Once the single strands of the DNA have hybridized with the primers (that is, the primers have connected to the DNA single strands and in extension of the primers new DNA double strands are formed), the corresponding DNA partial sequence is amplified.

The ultra-high sensitivity places enormous demands on the preparation of the serum and the purification of the serum from residual molecules. That's not possible to 100%. Residual parts in the serum sample may well include millions of other molecules, if not more. Then the primers may hybridize with possibly homologous DNA sequences as well. For this reason, it seems plausible that many putative HI virus RNA sequences, that have been uploaded in the gene databases, have nothing to do with HIV.

There is another aspect: the following excerpt from the self-test questions in the **textbook** „*Biochemistry*“, 5th Edition, Berg, Tymoczko, Stryer, cf. https://www.ncbi.nlm.nih.gov/books/NBK22409/

*„**7. A blessing and a curse**. The power of PCR can also create problems. Suppose someone claims to have isolated dinosaur DNA by using PCR. What questions might you ask to determine if it is indeed dinosaur DNA?*

Answer: PCR can amplify as little as one molecule of DNA, statements claiming the isolation of ancient DNA need to be greeted with some skepticism. The DNA would need to be sequenced. Is it similar to

***human, bacterial, or fungal DNA? If so, contamination is the likely source of the amplified DNA**. Is it similar to that of birds or crocodiles? This sequence similarity would strengthen the case that it is dinosaur DNA, because these species are evolutionarily close to dinosaurs."*

Why should this problem only apply to suspected dinosaur DNA and not to all other species? Cf.

- Haist et al. „ *Reactivities of HIV-1 gag-Derived Peptides with Antibodies of HIV-1-Infected and Uninfected Humans*", AIDS RESEARCH AND HUMAN RETROVIRUSES, Vol 8, No 11, 1909:1917, **(1992)** https://epub.uni-regensburg.de/20412/1/wolf11.pdf

*"**Amino acid sequence comparison of HIV-1 gag proteins with those of human endogenous retroviruses (ERV K10, ERV 3) revealed significant similarities** predominantly in the domains showing elevated antibody cross-reactions."*

*„The fact, that HIV- sera show cross-reactivities especially with those protein regions that also show enhanced reactivities in HIV-1+ serum samples implies that similar sequences have already **been exposed to the immune system prior to HIV infection**." (p. 1915)*

- Parmentier et al., "*Epitopes of human immunodeficiency virus regulatory proteins tat, nef, and rev are expressed in normal human tissue*", American Journal of Pathology, 141 (**1992**) 1209-16, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1886654/

"*A marked staining with **anti- HIV-1-tat, anti-nef, and anti-rev, and anti-HIV-2-tat anti-bodies was found in a variety of cell types in different organs from uninfected individuals***."

- Lyden et al., "*Expression of endogenous HIV-1 cross-reactive antigens within normal human extravillous trophoblast cells*", Journal of Reproductive Immunology, 28 (**1995**) 233-45, https://www.ncbi.nlm.nih.gov/pubmed/7473433

- Faulk et al. „*HIV proteins in **normal** human placentae*", Am J Reprod Immunol. **1991** Apr;25(3):99-104, https://www.ncbi.nlm.nih.gov/pubmed/1930645

This publications show what ultra-high demands PCR places on the purification of the samples. At the same time, they are part of a branch of research that nobody is persuing anymore. So much is known thanks to PCR.

The method is incredibly sensitive, but not specific. It goes so far that DNA components of foods that enter the serum from the intestinal tract can be detected. One molecule is enough.

This method was used without the limitations and weaknesses of this ultra-high sensitivity having been sufficiently explored. Of course, the manufacturers are happy about the business. And WHO supports the worldwide expansion of PCR for HIV diagnosis while at the same time reducing the number of CD4 cell count facilities (see above, Doherty, WHO **2015**). Here further diagnostic disasters are possible, in addition to the HIV / AIDS problem.

Here are some publications on the problem area mentioned, cf.

- Boyd et al., "*False-positive polymerase chain reaction results for human papillomavirus in lichen planus. Potential laboratory pitfalls of this procedure.*", J Am Acad Dermatol. **1996** Jul;35(1):42-6, https://www.ncbi.nlm.nih.gov/pubmed/8682962

"*Accurate evaluation of tissue with PCR is difficult because of the procedure's profound sensitivity.* ***Positive results reported in the literature should be viewed with caution****. Potential causes for false-positive and false-negative results should be considered*."

- Ali et., "*False positivity of serological tests for hepatitis C virus.*", J Ayub Med Coll Abbottabad. **2010** Apr-Jun;22(2):43-5, https://www.ncbi.nlm.nih.gov/pubmed/21702264

"*Out of a total 254 anti HCV positive patients, 211 had viremia by RT-PCR. The false positivity noted was 16.9%*."

What is right now? The serological tests or the RT-PCR?

- Rupp et al., "*Be aware of the possibility of false-positive results in single-locus PCR assays for methicillin-resistant Staphylococcus aureus.*", J Clin Microbiol. **2006** Jun;44(6):2317, https://www.ncbi.nlm.nih.gov/pubmed/16757652

"*In conclusion, users of "single-locus" PCR assays for MRSA should be aware of the possibility of false-positive reactions. Nevertheless, the opportunity to rapidly screen potential MRSA carriers by nasal swabs and, thus, to prevent further nosocomial spread will* ***probably outweigh this disadvantage***."

- Incerti, Ghidini, "*False-positive diagnosis of intrauterine herpes simplex type 1 infection using PCR.*", Prenat Diagn. **2006** Aug;26(8):749-50, https://www.ncbi.nlm.nih.gov/pubmed/16865739

- Trinker et al., "*False-positive diagnosis of tuberculosis with PCR.*", Lancet. **1996** Nov 16;348(9038):1388, https://www.ncbi.nlm.nih.gov/pubmed/8918304

"*As amplification of mycobacterial DNA by PCR is increasingly used as a routine method, we would like to emphasise that this test should be applied with great caution in clinical medicine. In certain situations the* ***uncritical interpretation of PCR results might even be harmful to the patient*****."**

- Rolain et al., "*False positive PCR detection of Tropheryma whipplei in the saliva of healthy people*.", BMC Microbiol. **2007** May 29;7:48, https://www.ncbi.nlm.nih.gov/pubmed/17535423

"*Testing the specificity of designed primers is critical to avoid false positive detection of T. whipplei. In a typical case we recommend to test two different specific target genes before concluding."*

- Goyo et al., "*False-positive PCR detection of Tropheryma whipplei in cerebrospinal fluid and biopsy samples from a child with chronic lymphocytic meningitis*.", J Clin Microbiol. **2009** Nov;47(11):3783-4, https://www.ncbi.nlm.nih.gov/pubmed/19741072

"*We report the case of a teenager with chronic lymphocytic meningitis for whom Tropheryma whipplei 16S rRNA PCR results were positive in two cerebrospinal fluid samples and one duodenal biopsy specimen.* ***PCR targeting another specific sequence of Tropheryma whipplei and sequencing of the initially amplified 16S rRNA fragment did not confirm the results.***"

- Fetzer et al., "*High risk of false positive results in a widely used diagnostic test for detection of the porcine reproductive and respiratory syndrome virus (PRRSV).*", Vet Microbiol. **2006** Jun 15;115(1-3):21-31. Epub **2006** Feb 3, https://www.ncbi.nlm.nih.gov/pubmed/16458457

„*However, the primers published by Oleksiewicz were shown to yield a very high proportion of false positive results under routine diagnostic laboratory conditions, i.e. they resulted in RT-PCR products with non-PRRSV sequences, that were indistinguishable from truly positive reagents in standard gel electrophoresis settings.*"

- Kim et al., "*Discrepancies between Antigen and Polymerase Chain Reaction Tests for the Detection of Rotavirus and Norovirus.*", Ann Clin Lab Sci. **2016** May;46(3):282-5, https://www.ncbi.nlm.nih.gov/pubmed/27312553

"*Discrepant results between ELISA and PCR were common, and the* ***possibility of false-positive and false-negative results should be considered with rotavirus and norovirus assays****."*

- Nowrouzian et al., "*High frequency of false-positive signals in a real-time PCR-based "Plus/Minus" assay.*", APMIS. **2009** Jan;117(1):68-72, https://www.ncbi.nlm.nih.gov/pubmed/19161539

"*When testing the "Plus/Minus" assay for detection of usp genes encoding a uropathogenic specific protein in Escherichia coli,* ***an inordinately high proportion of false-positive signals was observed****. This was shown to be due to a serious methodological deficiency."*

- Agüero et al., "*False-positive results obtained when bluetongue virus serotype 1 Algeria 2006 was analyzed with a reverse transcription-PCR protocol for detection of epizootic hemorrhagic disease virus.*", J Clin Microbiol. **2008** Sep;46(9):3173-4, https://www.ncbi.nlm.nih.gov/pubmed/18596148

"*During the analysis of the bluetongue virus serotype 1 (BTV-1) strain Algeria 2006 grown in Vero cells at our laboratory (Laboratorio Central de Veterinaria [LCV]), false-positive results for epizootic hemorrhagic disease virus (EHDV) were detected when the reverse transcription-PCR (RT-PCR) technique previously described by Aradaib et al. was used.*"

- Moison et al., "*Commercial reverse transcriptase as source of false-positive strand-specific RNA detection in human cells.*", Biochimie. **2011** Oct;93(10):1731-7, https://www.ncbi.nlm.nih.gov/pubmed/21689721

"A commonly used technique to investigate the expression of an antisense ncRNAs is strand-specific reverse transcription coupled with polymerase chain reaction (RT-PCR). The advantage of this accurate technique is that it does not require any special equipment or expertise. ***The disadvantage is that it can lead easily to false-positive results****."*

- Aller-Morán et al. "*Cross-reactions in specific Brachyspira spp. PCR assays caused by "Brachyspira hampsonii" isolates: implications for detection*.", J Vet Diagn Invest. **2016** Nov;28(6):755-759, https://www.ncbi.nlm.nih.gov/pubmed/27664096

"However, ***the percentage of false-positive results varied, with a range of 10-80%****, in the evaluated B. hyodysenteriae-specific assays based on the amplification of the 23S rRNA, nox, and tlyA genes. Similarly, results of the B. intermedia-specific PCR assays yielded poor specificity,* ***with up to 80% of the "B. hampsonii" isolates tested giving false-positive results.****"*

- Czurda et al. "*Occurrence of Fungal DNA Contamination in PCR Reagents: Approaches to Control and Decontamination.*", J Clin Microbiol. **2016** Jan;54(1):148-52, https://www.ncbi.nlm.nih.gov/pubmed/26560539

"Traces of fungal DNA were found in different commercially available PCR reagents, including lyophilized primers, TaqMan probes, and master mix solutions. ***These contaminants resulted in a considerable rate of false-positive tests in panfungal real-time PCR analysis.****"*

- Bhaskaran et al., "*Interpretation of positive molecular tests of common viruses in the cerebrospinal fluid*.", Diagn Microbiol Infect Dis. **2013** Nov;77(3):236-40, https://www.ncbi.nlm.nih.gov/pubmed/24035384

"*A positive CSF viral PCR result has to be interpreted with caution due to several false-positive results."*

- Maass et al., "*Sequence homologies between Mycoplasma and Chlamydia spp. lead to false-positive results in chlamydial cell cultures tested for mycoplasma contamination with a commercial PCR assay*.", J Clin Microbiol. **2011** Oct;49(10):3681-2, https://www.ncbi.nlm.nih.gov/pubmed/21849688

"After obtaining contradictory contamination results, we compared three commercial PCR kits for mycoplasma detection. One kit signaled contamination in mycoplasma-free Chlamydia pneumoniae cultures. ***Sequencing of cloned PCR products revealed primer homology with the chlamydial genome as the basis of this false-positive result.****"*

- Dijkstra et al., "*Critical appraisal of quantitative PCR results in colorectal cancer research: can we rely on published qPCR results*?", Mol Oncol. **2014** Jun;8(4):813-8, https://www.ncbi.nlm.nih.gov/pubmed/24423493

"*Consequently, we assessed all colorectal cancer publications that made use of qPCR from 2006 until August 2013 for the number of reference genes used and whether they had been validated.* ***Using even these minimal evaluation criteria, the validity of only three percent (6/179) of the publications can be adequately assessed****. We describe common errors, and conclude that the current state of reporting on qPCR in colorectal cancer research is* ***disquieting.****"*

Here is a publication that food supplements or contaminants of food supplements (fungi) can lead to positive reactions in the PCR in sick people with gastrointestinal diseases.

- Millon et al., "*False-positive Aspergillus real-time PCR assay due to a nutritional supplement in a bone marrow transplant recipient with GVH disease*.", Med Mycol. **2010** Jun;48(4):661-4, https://www.ncbi.nlm.nih.gov/pubmed/20392146

"*False positives for Aspergillus real-time PCR assays have been described in several reports, but no sources of fungal DNA contamination could be clearly identified. We report a false-positive case for both galactomannan (GM) antigenemia and Aspergillus PCR due to nutritional supplement intake in a bone marrow transplant recipient with digestive graft-versus-host disease.* ***Our case report also suggests that fungal DNA can pass into the serum from the intestinal tract in the same way as fungal GM***."

"Therefore, the most probable hypothesis is that the Aspergillus DNA present in the ***nutritional supplement passed through the mucosa, in an amount large enough to be detected in serum.****"*

There are other examples that DNA transgresses from the digestive system into the blood and is detectable there, cf.

- Spisák et al., "*Complete genes may pass from food to human blood*.", PLoS One. **2013** Jul 30;8(7):e69805, https://www.ncbi.nlm.nih.gov/pubmed/23936105

"*Here, based on the analysis of over 1000 human samples from four independent studies, we report evidence that meal-derived DNA fragments which are large enough to carry complete genes can avoid degradation and through an unknown mechanism enter the human circulation system.* ***In one of the blood samples the relative concentration of plant DNA is higher than the human DNA***."

- Schubbert et al., "*Foreign (M13) DNA ingested by mice reaches peripheral leukocytes, spleen, and liver via the intestinal wall mucosa and can be covalently linked to mouse DNA*.", Proc Natl Acad Sci U S A. **1997** Feb 4;94(3):961-6, https://www.ncbi.nlm.nih.gov/pubmed/9023365

"*In 84 animals, fragments of M13mp18 DNA were detected in the contents of the small intestine, the cecum (until 18 h), the large intestine, or the feces. In 254 animals, M13mp18 DNA fragments of up to 976 bp were found in blood 2-8 h after feeding. In buffer-fed control animals, M13mp18 DNA could not be detected.*"

"*M13mp18 DNA could be traced by fluorescent in situ hybridization in the columnar epithelial cells, in the leukocytes in Peyer's patches of the cecum wall, in liver cells, and in B cells, T cells, and macrophages from spleen.* ***These findings suggest transport of foreign DNA through the intestinal wall and Peyer's patches to peripheral blood leukocytes and into several organs***."

It should also be noted: in PCR, less than 10 molecules that pass into the serum are sufficient. This makes the results of Romero (2014) appear in a different light.

And of course there is the problem that PCR cannot differentiate between living and dead cells (or cell or viral fragments):

- Wolffs et al., *„Risk assessment of false-positive quantitative real-time PCR results in food, due to detection of DNA originating from dead cells.",* J Microbiol Methods. **2005** Mar, 60(3):315-23, https://www.ncbi.nlm.nih.gov/pubmed/15649533

"Based on these results, it was concluded that, especially in pork samples, there is a risk of false-positive PCR results. This was confirmed in a quantitative study on cell death and signal persistence over a period of 28 days, employing three different methods, i.e. viable counts, direct qPCR, and finally floatation, a recently developed discontinuous density centrifugation method, followed by qPCR. ***Results showed that direct qPCR resulted in an overestimation of up to 10 times of the amount of cells in the samples compared to viable counts, due to detection of DNA from dead cells.****"*

What is the impact of this problem on HIV viral load (see below)? Which of the supposedly counted viruses are even active? Apart from the problem that antibodies against HIV are present in the human body.

- Bennett et al., "*False positive influenza A and B detections in clinical samples due to contamination with live attenuated influenza vaccine*.", J Med Microbiol. **2015** Apr;64(Pt 4):466-8, https://www.ncbi.nlm.nih.gov/pubmed/25657303

"To conclude, our results highlight those laboratories using highly sensitive real-time PCR methods should be aware of the risk of LAIV contamination occurring within clinical samples taken at the time of vaccination protocols/roll out. ***Public health bodies should also be aware of this issue when interpreting laboratory surveillance data.***"

- Curran, "*False-positive PCR results linked to administration of seasonal influenza vaccine*.", J Med Microbiol. **2012** Mar;61(Pt 3):332-8, https://www.ncbi.nlm.nih.gov/pubmed/22096134

"***RNA detection studies demonstrated vaccine RNA still detectable for at least 66 days****. Administration of influenza vaccines and clinical sampling in the same room resulted in the contamination with vaccine strains of surveillance swabs collected from patients with ILI.* ***Vaccine contamination should therefore be considered, particularly where multiple influenza virus RNA PCR positive signals*** *(e.g. H1N1, H3N2 and influenza B) are detected in the same specimen."*

Sometimes human DNA gets in the way, cf. also above, Romero **2014**.

- Chan et al. „*False-positive PCR detection of cyclovirus Malawi strain VS5700009 in human cerebrospinal fluid.*", J Clin Virol. **2015** Jul;68:76-8, https://www.ncbi.nlm.nih.gov/pubmed/26071341

"*The original PCR assay for CyCV-VS5700009 detection may have* ***potential cross-reactivity with contaminating human genomic DNA****. The assay may be of little diagnostic use on clinical specimens that are rich in host DNA such as biopsy tissues.*"

In part, the non-specificity of PCR has found its way into the daily press. However, this remains the exception, cf.

- Gina Kolata, New York Times, "*Faith in Quick Test Leads to Epidemic That Wasn't*", Jan 22, **2007**, https://www.nytimes.com/2007/01/22/health/22whoop.html?sec=health&pagewanted=all

"*The big message is that every lab is vulnerable to having false positives," Dr. Petti said. "No single test result is absolute and that is* ***even more important with a test result based on P.C.R****."*

Overall, this does not give the impression of having the PCR method under control.

Here is an article from 2018 on the basic issue of prematurely introducing new technology into the research process:

- He et al., "*While it is not deliberate, much of today's biomedical research contains logical and technical flaws, showing a need for corrective action.*", Int J Med Sci. **2018** Jan 19;15(4):309-322, https://www.ncbi.nlm.nih.gov/pubmed/29511367

"*Biomedical research has advanced swiftly in recent decades, largely due to progress in biotechnology.* ***However, this rapid spread of new, and not always-fully understood, technology has also created a lot of false or irreproducible data and artifacts, which sometimes have led to erroneous conclusions****.*"

"***Another major reason is that we are too rushed in introducing new technology into our research*** *without assimilating technical details. In this essay, we provide examples in different research realms to justify our points. To help readers test their own weaknesses,* ***we raise questions on technical details of RNA reverse transcription, polymerase chain reactions, western blotting and immunohistochemical staining****, as these methods are basic and are the base for other modern biotechnologies.*"

"*Many scientists have successfully established their career at a young age by introducing novel techniques into their research areas and publishing in high-impact journals,* ***while leaving the research fields with numerous artifacts and biased or erroneous conclusions.****"*

In summary:

- DNA is DNA.
- Whatever the primers find to dock with, it will be amplified. This can also be DNA fragments of food molecules that have entered the serum. Or it is simply human DNA that is complementary to the primer, see above Romero, 2014, or Chan et al., 2015.
- Obviously, one is aware of the problem and is increasingly trying to use different primers in parallel. This leads to the question of whether the last 25 years the methodology has been developed at living objects. It does not help, as soon as a primers amplify the wrong signal, the measurement becomes obsolete. It only shows the weaknesses of the PCR methodology.
- PCR cannot differentiate between active and inactive cells or viruses.
- Manufacturers reject PCR for HIV diagnosis for a good reason.

All these findings have nothing to do with the question of what proportion of endogenous retroviral components are involved in the diagnosis (see above on HERV).

29. Annex III: Information on the correlation of MSM with classical infections and drug abuse

From hivbuch.de (Hoffmann und Rockstroh, HIV Buch 2016/17)
https://www.hivbuch.de/wp-content/uploads/2017/04/hiv2016-17_fix.pdf

29.1. Drug abuse

S. 11:
„Meist erkranken zunächst Personen aus so genannten Hochrisikogruppen (i.v. Drogengebraucher/-innen, Menschen in der Prostitution und Männer, die Sex mit Männern haben), wobei sich anschließend auch andere Personengruppen durch ungeschützten Sex anstecken.“

Translation:

„Mostly people from so-called high-risk groups get infected (i.v. drug users, people in prostitution and men who have sex with men), which then infect other groups through unprotected sex“

S. 173:
*„**Diese Drogen bzw. „Chemsex“ sind heute allgegenwärtig und fester Bestandteil im Leben vieler Patienten**. Der Begriff „Chemsex” beschreibt dabei sexuelle Kontakte unter dem Einfluss psychoaktiver Substanzen wie Mephedron, Crystal-Methamphetamin („Crystal Meth”, geraucht oder injiziert: „Slam“) und Gamma-hydroxybutyrat (Samsonit® oder „Liquid Ecstasy“, GHB, GBL). Diese illegalen Drogen erhöhen die Libido und reduzieren das Schlafbedürfnis.“*

Translation:

„These drugs or "chemsex" are now ubiquitous and an integral part in the lives of many patients. The term "chemsex" describes sexual contacts under the influence of psychoactive substances such as mephedrone, crystal methamphetamine ("Crystal Meth", smoked or injected: "Slam") and gamma-hydroxybutyrate (Samsonit® or "Liquid Ecstasy", GHB, GBL). These illegal drugs increase libido and reduce the need for sleep.“

S. 619:
*„**Wenigstens die Hälfte der Männer, die Sex mit Männern haben (MSM), berichten über Substanzgebrauch beim Sex** (ASTRA Studie 2014). Von den etwa 83.400 HIV positiven Menschen die Ende 2014 in Deutschland bekannt waren, gehörten etwa 7.900 (ca. 8 %) zur Gruppe der intravenösen Drogengebrauchenden (RKI 2015). Der intravenöse Drogengebrauch stellt nach wie vor einen wichtigen Risikofaktor für den Erwerb einer HIV-Infektion und einer Hepatitis-C-Koinfektion dar (Lucas 2011).“*

Translation:

„At least half of men who have sex with men (MSM) report substance use during sex (ASTRA Study 2014). Of the approximately 83,400 HIV positive people known in Germany at the end of 2014, around 7,900 (around

8%) belonged to the group of intravenous drug users (RKI 2015). Intravenous drug use remains an important risk factor for the acquisition of HIV infection and hepatitis C coinfection (Lucas 2011)"

*„**Speziell die Alkoholabhängigkeit ist ein Schädigungsfaktor** (Gruber 2010, Lopes 2011, Watkins 2011); die durch Ethanol ausgelöste Neurodegeneration wird als synergistisch mit der durch HIV selbst ausgelösten Neurodegeneration angesehen (Hahn 2010). Abhängiger Alkoholgebrauch ist zudem als Faktor bekannt, der die Mortalität bei HIV-Patienten erheblich erhöht (Obel 2011).“*

Translation:

„In particular, alcohol dependence is a factor of damage (Gruber 2010, Lopes 2011, Watkins 2011); Ethanol-induced neurodegeneration is considered to be synergistic with HIV-induced neurodegeneration (Hahn 2010). Dependent alcohol use is also known as a factor that significantly increases mortality in HIV patients (Obel 2011).“

S.626:
„*Neuerdings weisen Studien bei MSM auf die **Korrelation aus Einnahme von Drogen und PDE-5-Inhibitoren sowie riskantem Sexualverhalten** hin (Swearingen 2005, Purcell 2005, Spindler 2006, Dirks 2012).“*

Translation:

„Recently, studies in MSM indicate the correlation between drug use and PDE-5 inhibitors and risky sexual behavior (Swearingen 2005, Purcell 2005, Spindler 2006, Dirks 2012)“

29.2. Classical infections

S. 416:
„Aufgrund gleicher Transmissionswege kommen HIV/HCV-Doppelinfektionen häufig vor. In Deutschland sind etwa 10.000 (15 % aller HIV-Patienten), in den USA 240.000 Menschen (30 %) mit beiden Viren infiziert. In Ost-Europa sind die Raten häufig höher (Rockstroh 2005). So sind in Russland aufgrund der hohen Zahl von i.v.-Drogenkonsumenten etwa 70 % der 940.000 HIV-Patienten zusätzlich HCV-positiv.“

Translation:

„Due to the same transmission pathways, HIV / HCV double infections are common. In Germany about 10,000 (15% of all HIV patients), in the US 240,000 people (30%) are infected with both viruses. In Eastern Europe, the rates are often higher (Rockstroh 2005). In Russia, due to the high number of i.v. drug users, about 70% of the 940,000 HIV patients are additionally HCV positive.“

S. 426:

*„**Bis zu 95 % aller HIV-infizierten Patienten haben eine Hepatitis B durchgemacht**, etwa 10–15 % haben eine chronische Hepatitis B.“*

Translation:

„Up to 95% of all HIV-infected patients have undergone hepatitis B, about 10-15% have chronic hepatitis B.“

S. 439:

*„**Bei ca. 45 % der neu diagnostizierten Syphilisinfektionen besteht gleichzeitig eine HIV-Infektion** (RKI 2010). Jeder Syphilis-Patient sollte auf HIV (unterschiedliche Inkubationszeiten!) untersucht werden, jeder HIV-Patient regelmässig auf Syphilis (Reinfektionen/Reaktivierungen).“*

Translation:

„In about 45% of newly diagnosed syphilis infections there is also an HIV infection (RKI 2010). Every syphilis patient should be screened for HIV (different incubation times!) And every HIV patient should be regularly screened for syphilis (reinfections / reactivations).“

30. Annex IV: Current and systematic problems in biomedical research

The questionable hypothesis *HIV=AIDS* fits into a larger context. As the numerous publications in the main section have shown, there are considerable doubts about the validity of this hypothesis. However, it is ***big business***.

The model as such, here the great threat, there the miracle medicine, was transferred to many other areas. However, the applied research methods are not free from criticism, better: not free from massive criticism.

This is largely lost in the public debate. The trust in science seems enormous. But after selling HIV serological self-tests to the public, it is somewhat astonishing that even well-equipped bio laboratories have enormous problems in verifying the specificity of the antibodies and antibody tests used (***reproducibility crisis***). At the same time, quantitative data obtained through ***qPCR*** remains frequently questionable. What does this mean for persons, presumed to be ill, who are subjected to these methods during the so called diagnosis?

Here is an overview of the current, systematic problems in biomedical research, in terms of

- the growing criticism of hastily introduced new methods (e.g., qPCR, also used for determining viral load),
- cross-contamination and misidentification of cell lines and
- the so-called antibody reproducibility crisis

For this we refer to the following selection of recent articles, cf.

30.1. Criticism of methods (including PCR for the determination of viral load)

- Bustin, Nolan, "*Talking the talk, but not walking the walk: RT-qPCR as a paradigm for the lack of reproducibility in molecular research.*", Eur J Clin Invest. **2017** Oct;47(10):756-774, https://www.ncbi.nlm.nih.gov/pubmed/28796277

*"**Poorly executed and inadequately reported molecular measurement methods are amongst the causes underlying the lack of reproducibility of much biomedical research.** Although several high impact factor journals have acknowledged their past failure to scrutinise adequately the technical soundness of manuscripts, there is a perplexing reluctance to implement basic corrective measures. The reverse transcription real-time quantitative PCR (RT-qPCR) is probably the most straightforward measurement technique available for RNA quantification and is widely used in research, diagnostic, forensic and biotechnology applications. Despite the impact of the minimum information for the publication of quantitative PCR experiments (MIQE) guidelines, which aim to improve the robustness and the transparency of reporting of RT-qPCR data, **we demonstrate that elementary protocol errors, inappropriate data analysis and inadequate reporting continue to be rife and conclude that the majority of published RT-qPCR data are likely to represent technical noise.**"*

- He et al., "*While it is not deliberate, much of today's biomedical research contains logical and technical flaws, showing a need for corrective action*.", Int J Med Sci. **2018** Jan 19;15(4):309-322, https://www.ncbi.nlm.nih.gov/pubmed/29511367

"Biomedical research has advanced swiftly in recent decades, largely due to progress in biotechnology. However, this rapid spread of new, and not always-fully understood, technology has also created a lot of false or irreproducible data and artifacts, which sometimes have led to erroneous conclusions. When describing various scientific issues, scientists have developed a habit of saying "on one hand… but on the other hand…", because discrepant data and conclusions have become omnipresent. One reason for this problematic situation is that we are not always thoughtful enough in study design, and sometimes lack enough philosophical contemplation. ***Another major reason is that we are too rushed in introducing new technology into our research without assimilating technical details. In this essay, we provide examples in different research realms to justify our points****. To help readers test their own weaknesses, we raise questions on technical details of RNA reverse transcription, polymerase chain reactions, western blotting and immunohistochemical staining, as these methods are basic and are the base for other modern biotechnologies."*

- Chatzimanouil et al., "*Quantity and Reporting Quality of Kidney Research*.", J Am Soc Nephrol. **2019** Jan;30(1):13-22, https://www.ncbi.nlm.nih.gov/pubmed/30545982

"Reporting quality analysis of preclinical studies revealed ***substantial reporting deficits across all leading journals, with little improvement over the last 20 years****, especially for group size calculations, defining primary versus secondary outcomes, and blinded analysis."*

- Hartung, "*Look back in anger - what clinical studies tell us about preclinical work*.", ALTEX. **2013**;30(3):275-91, https://www.ncbi.nlm.nih.gov/pubmed/23861075

Misled by animal studies and basic research? Whenever we take a closer look at the outcome of clinical trials in a field such as, most recently, stroke or septic shock, we see how limited the value of our preclinical models was. ***For all indications, 95% of drugs that enter clinical trials do not make it to the market, despite all promise of the (animal) models used to develop them****. Drug development has started already to decrease its reliance on animal models: In Europe, for example, despite increasing R&D expenditure, animal use by pharmaceutical companies dropped by more than 25% from 2005 to 2008.* ***In vitro studies are likewise limited: questionable cell authenticity, over-passaging, mycoplasma infections, and lack of differentiation as well as non-homeostatic and non-physiologic culture conditions endanger the relevance of these models****.* ***The standards of statistics and reporting often are poor, further impairing reliability.*** *Alarming studies from industry show miserable reproducibility of landmark studies.*

- Prager et al., "*Improving transparency and scientific rigor in academic publishing*.", Brain Behav. **2019** Jan;9(1):e01141, https://www.ncbi.nlm.nih.gov/pubmed/30506879

"Progress in basic and clinical research is slowed when researchers fail to provide a complete and accurate report of how a study was designed, executed, and the results analyzed. Publishing rigorous scientific research involves a full description of the methods, materials, procedures, and outcomes. Investigators may

fail to provide a complete description of how their study was designed and executed because they may not know how to accurately report the information or the mechanisms are not in place to facilitate transparent reporting. ***Here, we provide an overview of how authors can write manuscripts in a transparent and thorough manner****."*

That sounds helpful, as of **2019**.

- Al-Ani et al., "*Oxygenation in cell culture: Critical parameters for reproducibility are routinely not reported.*", PLoS One. **2018** Oct 16;13(10):e0204269, https://www.ncbi.nlm.nih.gov/pubmed/30325922

"On analyzing two hundred articles from high-impact journals we find a large majority missing at least one key piece of information necessary to ensure consistency in replication."

- Sanders et al. "*Improving the standardization of mRNA measurement by RT-qPCR*", Biomol Detect Quantif. **2018** May; 15: 13–17, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6006386/

"Our recent review of the literature has shown that the qPCR data underlying the vast majority of publications reporting use of this technique are, at the very least, inadequately reported and that the peer review process allows the publication of ***incomplete experimental protocols, yielding results that are difficult to evaluate independently.*** *An analysis of all colorectal cancer publications that made use of qPCR between 2006 and 2013 shows* ***that only 3% (n=179) report sufficient experimental detail to allow a reliable assessment of the qPCR data****. That paper also showed that 92% of publications used a single reference gene,* ***with 13% validating its use and 92% of papers use a method of analysis that is meaningless unless PCR efficiencies are known, yet 82% do not mention PCR efficiency****. A more recent analysis found that 95% of papers (n=20) used a single reference gene for normalisation, with only 20% using a single validated reference gene.* ***Two other surveys found that 100% of papers (n=20) used inappropriate analysis and normalisation procedures****."*

- Dijkstra et al., "*Critical appraisal of quantitative PCR results in colorectal cancer research: can we rely on published qPCR results*?", Mol Oncol. **2014** Jun;8(4):813-8, https://www.ncbi.nlm.nih.gov/pubmed/24423493

"The use of real-time quantitative polymerase chain reaction (qPCR) in cancer research has become ubiquitous. The relative simplicity of qPCR experiments, which deliver fast and cost-effective results, means that each year an increasing number of papers utilizing this technique are being published. But how reliable are the published results?"

"We describe common errors, and conclude that the current state of reporting on qPCR in colorectal cancer research is disquieting. ***Extrapolated to the study of cancer in general, it is clear that the majority of studies using qPCR cannot be reliably assessed and that at best, the results of these studies may or may not be valid and at worst, pervasive incorrect normalisation is resulting in the wholesale publication of incorrect conclusions****."*

30.2. Cross-contamination of cell lines in biomedical research

- Alexandra del Carpio „*The good, the bad, and the HeLa*", Berkeley Science Review, April 27, **2014**, http://berkeleysciencereview.com/article/good-bad-hela/

"The survey also revealed that about 10% of respondents still used HeLa contaminants, 30% of which used them for tissue-specific purposes. The original "HeLa bomb" of the 1960s and 70s had lingering effects, it appeared."

- Jill Neimark, "*Line of attack*", Science Mag, Feb, 27, **2015**, Vol 347, Issue 6225, https://www.jillneimark.com/pdf/line-of-attack.pdf

"Christopher Korch estimated the impact of research on two cell lines, HEp-2 and INT 407. Due to contamination long ago, both are now widely acknowledged to be composed of cancer cells called HeLa. ***5789 ARTICLES*** *in* ***1182 journals*** *may have used HEp-2 inappropriately, producing an estimated 174,000 citations.* ***1336 ARTICLES*** *in* ***271 journals*** *may have used INT 407 inappropriately, producing an estimated 40,000 citations."*

- Rojas et al. "*Cell line cross-contamination in biomedical research: a call to prevent unawareness*.", Acta Pharmacol Sin. **2008** Jul;29(7):877-80, https://www.ncbi.nlm.nih.gov/pubmed/18565286

"During the 1950s, cross-contamination of cell lines emerged as a problem with serious consequences on the quality of biomedical research. ***Unfortunately, this situation has worsened over years****. In this context, some actions should be urgently undertaken to avoid the generation of misleading data due to the increasingly and sometimes neglected use of cross-contaminated cell lines."*

- Buehring et al., "*Cell line cross-contamination: how aware are Mammalian cell culturists of the problem and how to monitor it?*", In Vitro Cell Dev Biol Anim. **2004** Jul-Aug;40(7):211-5, https://www.ncbi.nlm.nih.gov/pubmed/15638703

"Over 220 publications were found in the PubMed database (1969-2004) in which HeLa contaminants were used as a model for the tissue type of the original cell line. Overall, the results of this study indicate a lack of vigilance in cell acquisition and identity testing. ***Some researchers are still using HeLa contaminants without apparent awareness of their true identity***."

- Porwollik, „*The Cell Line Cross-Contamination Crisis, Part I: Know Your Problem*", Biocision, Jan 19, **2016**, http://www.biocision.com/blog/12729/cell-line-cross-contamination-crisis-one

*"****Alarmingly, such cell line cross-contaminations have become endemic, with over 450 currently used cell lines (and an estimated 15% of all human cell lines) in modern research known to be cross-contaminated.*** *Even more frighteningly, many researchers do not know whether cell line cross-contamination has affected their cell line of choice, and obliviously proceed with their research using corrupted cells. This is a disaster for scientific progress, allocation of research funding and therapy development."*

- Horbach et al., "*The ghosts of HeLa: How cell line misidentification contaminates the scientific literature.*", PLoS One. **2017** Oct 12;12(10):e0186281, https://www.ncbi.nlm.nih.gov/pubmed/29023500

"While problems with cell line misidentification have been known for decades, an unknown number of published papers remains in circulation reporting on the wrong cells without warning or correction. Here we attempt to make a conservative estimate of this 'contaminated' literature. ***We found 32,755 articles reporting on research with misidentified cells, in turn cited by an estimated half a million other papers.*** *The contamination of the literature is not decreasing over time and is anything but restricted to countries in the periphery of global science. The decades-old and often contentious attempts to stop misidentification of cell lines have proven to be insufficient."*

- Teixeira da Silva et al., "*Incorrect cell line validation and verification*.", Ann Transl Med. **2018** Apr;6(7):136, https://www.ncbi.nlm.nih.gov/pubmed/29955596

*"**There is increasing evidence, however, that globally, a large number of cell lines have become contaminated**, either as a result of poor laboratory and cell line management, or cross-contamination by other cell lines, either of the same species or another species (1), with human cervical adenocarcinoma, or HeLa cells, having the most number of contaminated lines, 106 (2)."*

"As one example, Christopher Korch, a geneticist, estimated that contamination of HEp-2 and INT 407 cell lines by HeLa cells may have affected the published literature as follows: ***5,789 papers in 1,182 journals and 1,336 papers in 271 journals may have used HEp-2 and INT 407 cell lines, respectively, inappropriately, thereby affecting hundreds of thousands of citations and possibly billions of US dollars in follow-up research*** *that may be erroneously based on the wrong or cross-contaminated cell line (3)."*

- Huang et al., "*Investigation of Cross-Contamination and Misidentification of 278 Widely Used Tumor Cell Lines*", PLoS One. **2017**; 12(1): e0170384, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5249119/

"*In this study, we present a comprehensive investigation of cross-contamination and misidentification for a panel of 278 cell lines from 28 institutes in China by using short tandem repeat profiling method. By comparing the DNA profiles with the cell bank databases of ATCC and DSMZ,* ***a total of 46.0% (128/278) cases with cross-contamination/misidentification were uncovered coming from 22 institutes.*** *Notably, 73.2% (52 out of 71) of the cell lines established by the Chinese researchers were misidentified and accounted for 40.6% of total misidentification (52/128). Further, 67.3% (35/52) of the misidentified cell lines established in laboratories of China were HeLa cells or a possible hybrid of HeLa with another kind of cell line."*

- Eckers et al., "*Identity Crisis - Rigor and Reproducibility in Human Cell Lines*.", Radiat Res. **2018** Jun;189(6):551-552, https://www.ncbi.nlm.nih.gov/pubmed/29652622

"Cell line identity (more precisely, misidentification) has become a major source of concern for funding agencies, conscientious investigators, publishers and pharmaceutical companies. ***Worldwide, up to one-half of commonly used cell lines are believed to be misidentified."***

As of **2018**.

30.3. Reproducibility crisis in antibodies

- Vasilevsky et al., "*On the reproducibility of science: unique identification of research resources in the biomedical literature*.", PeerJ. **2013** Sep 5;1:e148, https://www.ncbi.nlm.nih.gov/pubmed/24032093

*"**The results of this experiment show that 54% of resources are not uniquely identifiable in publications, regardless of domain, journal impact factor, or reporting requirements.** For example, in many cases the organism strain in which the experiment was performed or antibody that was used could not be identified. Our results show that identifiability is a serious problem for reproducibility."*

- Weller, "*Quality Issues of Research Antibodies*.", Anal Chem Insights. **2016** Mar 20;11:21-7, https://www.ncbi.nlm.nih.gov/pubmed/27013861

*"**According to several recent studies, an unexpectedly high number of landmark papers seem to be not reproducible by independent laboratories**. Nontherapeutic antibodies used for research, diagnostic, food analytical, environmental, and other purposes play a significant role in this matter. Although some papers have been published offering suggestions to improve the situation, they do not seem to be comprehensive enough to cover the full complexity of this issue. In addition, no obvious improvements could be noticed in the field as yet."*

- Weller, "*Ten Basic Rules of Antibody Validation*.", Anal Chem Insights. **2018** Feb 8;13:1177390118757462, https://www.ncbi.nlm.nih.gov/pubmed/29467569

*"**The quality of research antibodies is an issue for decades**. Although several papers have been published to improve the situation, their impact seems to be limited."*

- Helsby et al., "*Reporting research antibody use: how to increase experimental reproducibility*", Version 2. F1000Res. **2013** Jul 10 [revised 2013 Aug 23];2:153. doi: 10.12688/f1000research.2-153.v2, https://www.ncbi.nlm.nih.gov/pubmed/24358895

*"Research antibodies are used in a wide range of bioscience disciplines, yet it is common to hear dissatisfaction amongst researchers with respect to their quality. Although blame is often attributed to the manufacturers, scientists are not doing all they can to help themselves. **One example of this is in the reporting of research antibody use. Publications routinely lack key details, including the host species, code number and even the company who supplied the antibody**."*

- Voskuil , "*The challenges with the validation of research antibodies*", F1000Research **2017**, 6:161, Mar **2017**, https://f1000research.com/articles/6-161/v1

"***Everyone agreed that to some extent bad quality antibodies may contribute to lack of scientific progress and that something had to be done to remove such blame from the industries.*** *The strong message is that antibodies need proper validation first before being used in scientific research."*

- Pauly et al., "*How to avoid pitfalls in antibody use*.", F1000Res. **2015** Sep 7;4:691, https://www.ncbi.nlm.nih.gov/pubmed/26834988

*"Antibody use is ubiquitous in the biomedical sciences. However, determining best research practices has not been trivial**. Many commercially available antibodies and antibody-conjugates are poorly characterized and lack proper validation**. Uncritical application of such useless tools has contributed to the reproducibility crisis in biomedical research."*

- Delpire et al., "*Research antibodies: do not use them to stain your reputation.*", Am J Physiol Cell Physiol. **2015** Dec 1;309(11):C707-8, https://www.ncbi.nlm.nih.gov/pubmed/26628686

*"In a recent roundtable organized by the Federation of American Societies For Experimental Biology (FASEB) on data reproducibility and antibodies (8), we learned how the sale and use of antibodies place both basic and preclinical research at risk of losing support from the public at large, from funding agencies, and from Congress. **Hundreds of millions of dollars are wasted annually on poor data collected with nonvalidated antibodies (3)**.*

That sounds very alarming. One may also ask, what was the status in the mid-1980s, when the foundations for these developments were laid?

31. Annex V: on the question of CCR5-Delta32 gene defect and HIV immunity

The HIV / AIDS panic also allows for experiments that are far beyond the ethical boundaries of what medicine and bio-research should or should not do. But who cares? After all, this is about saving the world.

Examples of this are the genetically modified babies of US scientist Dr. *Jiankui He*. He genetically modified 2 human fertilized eggs to alter the gene for the CCR5 co-receptor so that the cells can no longer form an effective CCR5 co-receptor.

Remark:

The CCR5 gene encodes a co-receptor on the cell surface which, according to the current state of research, is necessary for the entry of the putative HI virus into the human host cells. If this gene is defective, the cell cannot form a functional CCR5 co-receptor (homozygous) or only restricted (heterozygous). Every human cell, apart from sperm and egg cells, has a double set of genes (diploidy). Heterozygous and homozygous refers to whether both genes encode the same phenotype. In a CCR5-Delta32 heterozygous (homozygous) human, he/she has a gene with the gene defect and a gene without the gene defect (two genes with the gene defect).

The hypothesis is proven to be wrong and not even close to the truth, as a glance at the literature shows. However, this hypothesis is further asserted and in 2019 it has received new support through the alleged healing of an HIV+ measured human, cf.

- Gupta et al. "*HIV-1 remission following CCR5Δ32/Δ32 haematopoietic stem-cell transplantation.*" Nature (**2019**), https://www.nature.com/articles/s41586-019-1027-4.epdf

Bone marrow was transplanted into an HIV+ person suffering from lymphoma (Hodgkin's lymphoma). The peculiarity was that the donor had the ***CCR5-Delta32 gene defect***. Note, as so often, we talk about HIV, not AIDS. *Hodgkin's lymphoma* is not AIDS defining.

We investigated 2 questions based on the biomedical literature:

a) Does the *CCR5-Delta32 gene defect* mean immunity to HIV?

Answer: **No**.

b) Do HIV+ *Long-Time-Non-Progressors* (LTNP) have the *CCR5-Delta32 gene defect*?

Answer: **No**.

It should be noted in the remarks below that here we do not discuss the question of whether the putative HI virus is the cause of AIDS. This is assumed since 1984, when *HIV=AIDS* was proclaimed, despite all the unanswered questions.

However, this does not prevent from discussing the inconsistencies and misconceptions in the context of the CCR5-Delta32 theses. This is particularly the case for the frequently described, presumed ***latent HIV***

reservoirs, which seem to be absent or irrelevant in the case of the cured cancer patient. Nevertheless, they are the justification for the ***lifelong therapy*** of HIV+ measured persons.

It should also be noted that these experiments take place at the molecular level and study there smallest fragments of genes. Thus, a conceivably small part of the human body is considered.

And last but not least, HIV/AIDS in HIV+ people in clinical context and in clinical trials, with a few exceptions, refers to people on HAART.

a) Does the CCR5-Delta32 gene defect mean immunity to HIV?

There is extensive literature showing that people who are heterozygous or homozygous for the CCR5-Delta32 gene defect can be measured HIV+, cf.

- Theodorou et al., "*HIV-1 infection in an individual homozygous for CCR5 delta 32. Seroco Study Group*.", Lancet. **1997** Apr 26;349(9060):1219-20, https://www.ncbi.nlm.nih.gov/pubmed/9130946

"Entry of HIV-1 into human cells requires CD4 and a coreceptor. CC-ehemokine receptor 5 (CCR-5) is the common coreceptor for macrophage-tropic, non-syncytium inducing (NSI) HIV-1 strains that predominate during initial infection. A 32 base-pair deletion (Δ32) in the CCR5 coding region results in a non-functional receptor. ***We describe a patient who was homozygous for CCR5 Δ32, but nonetheless became infected with HIV-1."***

- Balotta et al., "*Homozygous delta 32 deletion of the CCR-5 chemokine receptor gene in an HIV-1-infected patient.*", AIDS. **1997** Aug;11(10):F67-71, https://www.ncbi.nlm.nih.gov/pubmed/9256936

"RESULTS: ***The wild-type/delta 32 heterozygous and delta 32/delta 32 homozygous conditions were represented in 10.7 and 0.8% of healthy controls and in 9.8 and 0.7% of HIV-1-infected subjects, respectively****. Of note, the delta 32/delta 32 deletion of the CCR-5 gene was detected by PCR and sequencing confirmed in a patient with progressive infection harbouring a clade B virus with SI phenotype.*

CONCLUSIONS: ***delta 32/delta 32 homozygosity for the CCR-5 gene does not confer absolute protection against HIV-1 infection****, suggesting that either macrophage-tropic viral strains could use coreceptors other than CCR-5 or infect independently of the presence of a functional CCR-5 coreceptor."*

- Wang et al., "*CCR5-delta 32 gene deletion in HIV-1 infected patients*.", Lancet. **1997** Sep 6;350(9079):742, https://www.ncbi.nlm.nih.gov/pubmed/9291932

"Our studies suggest that there may not be a strict correlation between protection from HIV-1 infection and homozygosity or heterozygosity of chemokine receptor CCR5. *The inheritance of a heterozygous CCR5 allele may not necessarily be protective in a sibling or a blood relative. There is a complex interplay between virus and the host, and the protection and long-term non-progression in some HIV-1 infected individuals may not be directly related to the ΔCCR5 genotype*."

- Philpott et al., "*HIV-1 coreceptor usage, transmission, and disease progression*.", Curr HIV Res. **2003** Apr;1(2):217-27, https://www.ncbi.nlm.nih.gov/pubmed/15043204

"HIV-1 strains transmitted in vivo generally use CCR5. Viruses that use CCR5 (R5 viruses) appear to be associated with relatively stable infection. ***Years after chronic infection is established, CXCR4 utilizing strains emerge in approximately 50% of infected individuals."***

- Naif et al., "*A human immunodeficiency virus type 1 isolate from an infected person homozygous for CCR5Delta32 exhibits dual tropism by infecting macrophages and MT2 cells via CXCR4*.", J Virol. **2002** Apr;76(7):3114-24, https://www.ncbi.nlm.nih.gov/pubmed/11884536

"Our study demonstrates the ability of certain strains of HIV to readily use CXCR4 for infection *or entry into macrophages, which is highly relevant to the pathogenesis of late-stage disease and presumably also HIV transmission."*

- Sheppard et al., "*HIV-1 infection in individuals with the CCR5-Delta32/Delta32 genotype: acquisition of syncytium-inducing virus at seroconversion.*", J Acquir Immune Defic Syndr. **2002** Mar 1;29(3):307-13, https://www.ncbi.nlm.nih.gov/pubmed/11873082

*"****Six HIV-1-infected Delta32/Delta32 patients have been reported. We report 2 additional Delta32/Delta32-infected individuals****, among 106 seroconverters in a vaccine preparedness study. Like the previous 6, these individuals experienced rapid CD4 decline****. However, taken together, the 8 patients have neither uniformly high virus load nor rapid progression to AIDS****."*

"These results further support the conclusion that Delta32-mediated resistance is incomplete *and is associated with acquisition of exclusively-X4 variants of HIV-1. The pathogenic potential of these viruses may be different from late-stage X4 virus or early X4 virus acquired by individuals with other CCR5 genotypes."*

- Zapata et al., "*Influence of CCR5 and CCR2 genetic variants in the resistance/susceptibility to HIV in serodiscordant couples from Colombia*.", AIDS Res Hum Retroviruses. **2013** Dec;29(12):1594-603, https://www.ncbi.nlm.nih.gov/pubmed/24098976

"Seventy HIV-1-exposed, but seronegative (HESN) individuals, 57 seropositives (SP), and 112 healthy controls (HC) were included."

*"****In conclusion, the CCR5-Δ32 allele is not responsible for HIV-1 resistance in this HESN group****; however, the CCR2-I allele could be protective, while the 29G allele might increase the likelihood of acquiring HIV-1 infection. HHG1 and the AGACCAC-CCR2-I-CCR5 wild-type haplotype might promote HIV-1 infection while HHF2 might be related to resistance."*

- Zachar et al., "*Genetic analysis reveals ongoing HIV type 1 evolution in infected human placental trophoblast*.", AIDS Res Hum Retroviruses. **1999** Dec 10;15(18):1673-83, https://www.ncbi.nlm.nih.gov/pubmed/10606090

"However, none of the followed parameters, including maternal age, disease stage, antiretroviral therapy, ***CCR5delta32 deletion status of the infant****, and viral genotype, could be associated with viral transmission."*

- Nkenfou et al. "*Distribution of CCR5-Delta32, CCR5 promoter 59029 A/G, CCR2-64I and SDF1-3'A genetic polymorphisms in HIV-1 infected and uninfected patients in the west region of Cameroon*.", BMC Res Notes. **2013** Jul 23;6:288, https://www.ncbi.nlm.nih.gov/pubmed/23880174

"Our data suggest that ***the CCR5-Delta32 cannot account for the protection*** *as it was completely absent in our population."*

- Heydarifard et al., "*Polymorphisms in CCR5Δ32 and Risk of HIV-1 Infection in the Southeast of Caspian Sea, Iran.*", Dis Markers. **2017**;2017:4190107, https://www.ncbi.nlm.nih.gov/pubmed/29209099

"Therefore according to this study, the frequency of the allele CCR5Δ32 indicates no significant difference between either groups (p = 0.18) and it sounds that ***the mentioned mutation in heterozygote people would not affect their susceptibility against HIV infection.****"*

- Smoleń-Dzirba et al., "*HIV-1 Infection in Persons Homozygous for CCR5-Δ32 Allele: The Next Case and the Review*.", AIDS Rev. **2017** Dec;19(4):219-230, https://www.ncbi.nlm.nih.gov/pubmed/28534889

"Data on HIV-1-infected patients homozygous for the CCR5-Δ32 allele, course of HIV-1 infection in these cases, and the infecting viral strains from current and all former reports on HIV-1 infection in CCR5-Δ32 homozygotes were gathered and compared. ***Identification of HIV-1-infected persons homozygous for CCR5-Δ32 supports the evidence that the lack of functional CC-chemokine receptor 5 at the cell surface does not confer absolute protection against HIV-1 infection****, […]"*

- Tan et al., "*Distribution of CCR5-Delta32, CCR5m303A, CCR2-64I and SDF1-3'A in HIV-1 infected and uninfected high-risk Uighurs in Xinjiang, China*.", Infect Genet Evol. **2010** Mar;10(2):268-72, https://www.ncbi.nlm.nih.gov/pubmed/19958843

"Our data suggest that the CCR5-Delta32, CCR2-64I and SDF1-3'A variants may ***have limited effect on protecting from HIV-1 infection in Uighurs****."*

- Wang et al. "*Population survey of CCR5 delta32, CCR5 m303, CCR2b 64I, and SDF1 3'A allele frequencies in indigenous Chinese healthy individuals, and in HIV-1-infected and HIV-1-uninfected individuals in HIV-1 risk groups*.", J Acquir Immune Defic Syndr. **2003** Feb 1;32(2):124-30, https://www.ncbi.nlm.nih.gov/pubmed/12571520

"Furthermore, we observed no significant differences in allele or genotypic frequencies between HIV-1-infected and HIV-1-uninfected groups from the Han ethnic group. Our finding is the first reporting that there is ***likely no effect of the examined polymorphisms in our study on HIV-1 transmission in the Chinese Han population****."*

- Adojaan et al., "*High prevalence of the CCR5Delta32 HIV-resistance mutation among Estonian HIV type 1-infected individuals*.", AIDS Res Hum Retroviruses. **2007** Feb;23(2):193-7, https://www.ncbi.nlm.nih.gov/pubmed/17331026/

"In an Estonian population the frequency of the CCR5Delta32 allele has been found to be among the greatest observed to date. Ironically, Estonia is concomitantly characterized by a very high HIV-1 prevalence. We compared the allele frequencies in a healthy control population to the HIV-positive group. ***The frequency of heterozygous individuals did not differ significantly between the HIV-positive group and the control population****."*

- Rugeles et al., "*Molecular characterization of the CCR 5 gene in seronegative individuals exposed to human immunodeficiency virus (HIV)*.", J Clin Virol. **2002** Jan;23(3):161-9, https://www.ncbi.nlm.nih.gov/pubmed/11595595/

"CONCLUSIONS: The screening of the entire coding region of the ccr5 gene in all ESN did not revealed no other mutations that could account for resistance to HIV-1 infection. ***Although the CCR5 molecule is the most important coreceptor for HIV-1, mutations in this gene do not account for most of the cases of natural resistance to this virus that have so far been reported.****"*

- Reiche et al., "*Frequency of CCR5-Delta32 deletion in human immunodeficiency virus type 1 (HIV-1) in healthy blood donors, HIV-1-exposed seronegative and HIV-1-seropositive individuals of southern Brazilian population*.", Int J Mol Med. **2008** Nov;22(5):669-75, https://www.ncbi.nlm.nih.gov/pubmed/18949389

*"****However, the low frequency of CCR5-Delta32 homozygosity observed among HIV-1-exposed seronegative individuals shows that the allele could not explain, by itself, the natural resistance to HIV-1 infection*** *and different mechanisms of protection against HIV-1 infection that must be involved in this population."*

- Veloso et al., "*Effect of TNF-alpha genetic variants and CCR5 Delta 32 on the vulnerability to HIV-1 infection and disease progression in Caucasian Spaniards*.", BMC Med Genet. **2010** Apr 26;11:63, https://www.ncbi.nlm.nih.gov/pubmed/20420684/

"The study group consisted of 423 individuals. Of these, 239 were uninfected (36 heavily exposed but uninfected [EU] and 203 healthy controls [HC]) and 184 were HIV-1-infected (109 typical progressors [TP] and 75 long-term nonprogressors [LTNP] of over 16 years' duration)."

*"****The CCR5 Delta 32 distribution was non-significantly different in HIV-1-infected patients with respect to the uninfected population (…) and in LTNP vs TP (…)****."*

So there are very well HIV+ measured people with the genetic defect. And this applies to countries as far apart as **Italy**, **USA**, **Australia**, **Denmark**, **Colombia**, **Cameroon**, **Iran**, **Poland**, **China**, **Estonia**, **Brazil** and **Spain**. It is unlikely that this is always the same line of the suspected HI virus.

Everything else, from which other illnesses these people may suffer, or not, is often not part of the investigation.

Note that in 90% of HIV+ measured people in industrialized countries (US, EU), we are talking about men from high-risk groups (e.g. MSM - men having sex with men), who often suffer from multiple infections due to sexually transmitted diseases, e.g. Herpes, HBV, syphilis, gonorrhea, etc. and are also often strongly drug-dependent.

In developing countries, HIV+ people are often exposed to classic infections such as malaria or tuberculosis (*AIDS defining*), parasites, malnutrition and heavy metal poisoning.

However, the scientific community has agreed on an interpretation, including how the suspected virus enters the host cell.

There is no evidence whatsoever that putative HI viruses that enter via the CCR5 co-receptor cannot switch to another co-receptor, e.g. CXCR4. On the contrary, there are many indications that a ***co-receptor switch*** happens regularly, cf.

- Mild et al., "*High intrapatient HIV-1 evolutionary rate is associated with CCR5-to-CXCR4 coreceptor switch.*", Infect Genet Evol. **2013** Oct;19:369-77, https://www.ncbi.nlm.nih.gov/pubmed/23672855

*"**In approximately 70% of individuals infected with HIV-1 subtype B, the virus switches coreceptor use** from exclusively CCR5 use (R5 virus) to either inclusion of or exclusively CXCR4 use (X4 virus) during infection."*

- Coetzer et al., "*Evolution of CCR5 use before and during coreceptor switching*.", J Virol. **2008** Dec;82(23):11758-66, https://www.ncbi.nlm.nih.gov/pubmed/18815295/

*"In about **half of infected individuals or more**, env evolution leads to expansion of the use of entry coreceptor from CCR5 alone to CCR5 and CXCR4."*

- Gray et al., "*Genetic and functional analysis of R5X4 human immunodeficiency virus type 1 envelope glycoproteins derived from two individuals homozygous for the CCR5delta32 allele*.", J Virol. **2006** Apr;80(7):3684-91, https://www.ncbi.nlm.nih.gov/pubmed/16537640

*"**The persistence of CCR5-using HIV-1 in two CCR5delta32 homozygotes suggests the conserved CCR5 binding domain of Env is highly stable and provides new mechanistic insights important for HIV-1 transmission and persistence**."*

- Henrich et al., "*Viremic control and viral coreceptor usage in two HIV-1-infected persons homozygous for CCR5 Δ32*.", AIDS. **2015** May 15;29(8):867-76, https://www.ncbi.nlm.nih.gov/pubmed/25730507

*"We identified **two HIV-infected CCR5(Δ32/Δ32) individuals among a cohort of patients with spontaneous control of HIV-1 infection without antiretroviral therapy** and determined coreceptor usage of the infecting viruses."*

"One participant had phenotypic evidence of X4 virus, had no known favorable human leukocyte antigen alleles, and appeared to be infected by minority X4 virus from a pool that predominately used CCR5 for entry. ***The second participant had virus that was unable to use CXCR4 for entry in phenotypic assay but was able to engage alternative viral coreceptors (e.g., CXCR6) in vitro.****"*

"CONCLUSION: Our study demonstrates that individuals may be infected by minority X4 viruses from a population that predominately uses CCR5 for entry, and ***that viruses may bypass traditional HIV-1 coreceptors (CCR5 and CXCR4) completely by engaging alternative coreceptors to establish and propagate HIV-1 infection****"*

b) Do HIV+ Long-Time-Non-Progressors (LTNP) have the CCR5-Delta32 gene defect?

It is often not known that a considerable number of people measured HIV+ never develop AIDS, so-called *long-time non-progressors* (LTNP). AIDS here in the sense of the 30+ catalog diseases, which are included in the AID syndrome (number of diseases, including prolonged fever and diarrhea, adjusted several times).

It should be noted that the number of LTNPs depends on the definition. It is often demanded that the slope of the CD4 cell number should never be negative (curve strictly monotonically increasing). Even the healthiest person hardly achieves that. A flu infection during the study period and the CD4 cell count decreases temporarily. If the CD4 cell count is then measured, this person does not count as LTNP. Using reasonable standards, the number of HIV+ measured LTNPs is > 20%.

These people do not take ART either. Nevertheless, thanks to unremitting pharmaceutical marketing, they are under considerable psychological pressure to finally take their "*medicine*".

There is no single genetic pattern that makes up these LTNPs, also not the CCR5-Delta32 gene defect.

- Nissen et al., "*Whole Exome Sequencing of HIV-1 long-term non-progressors identifies rare variants in genes encoding innate immune sensors and signaling molecules*", Sci Rep. **2018**; 8: 15253, https://www.ncbi.nlm.nih.gov/pubmed/30323326

"Common CCR5-Δ32 and HLA alleles only explain a minority *of the HIV long-term non-progressor (LTNP) and elite controller (EC) phenotypes."*

- Antoni et al., "Genetic and biological characterization of recombinant HIV type 1 with Env derived from long-term nonprogressor (LTNP) viruses.", AIDS Res Hum Retroviruses. 2007 Nov;23(11):1377-86, https://www.ncbi.nlm.nih.gov/pubmed/18184081

"Concerning the cellular factors, ***none of the eight LTNPs showed the 32-base pair deletion in the ccr5 gene*** *[…]."*

- Bendenoun et al., "*What Is the most Important for Elite Control: Genetic Background of Patient, Genetic Background of Partner, both or neither? Description of Complete Natural History within a Couple of MSM.*", EBioMedicine. **2018** Jan;27:51-60, https://www.ncbi.nlm.nih.gov/pubmed/29273355

"We describe a homosexual man who strongly controlled HIV-1 for ten years despite lack of protective genetic background."

"The patient and his partner were ***heterozygous for the CCR5ΔD32 deletion*** *[…]."*

- Gomes et al., "*Immunological and virological characterization of HIV-1 viremia controllers in the North Region of Brazil*.", BMC Infect Dis. **2017** Jun 1;17(1):381, https://www.ncbi.nlm.nih.gov/pubmed/28571570

"None of the individuals presented the CCR5Δ32– allele in homozygosis, *but it was present in heterozygosis in one individual of the NC group (Table 5)."*

- Chaudhuri et al., "*Genetic factors associated with slow progression of HIV among perinatally-infected Indian children*.", Indian Pediatr. **2014** Oct;51(10):801-3, https://www.ncbi.nlm.nih.gov/pubmed/25362010

"Among 165 children, 10 (6%) long-term non-progressors and 8 (5%) slow progressors were identified. For comparison, 12 children with normal progression of HIV were included. ***The frequencies of CCR5-Δ32 deletion, SDF1-3'A and CCR5-59029G did not differ significantly."***